

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
17 April 2003 (17.04.2003)

PCT

(10) International Publication Number
WO 03/031650 A2

(51) International Patent Classification⁷: **C12Q 1/68**

MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number: PCT/EP02/11034

(22) International Filing Date: 2 October 2002 (02.10.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0124145.4 8 October 2001 (08.10.2001) GB

(71) Applicant (for all designated States except US): **BAYER AKTIENGESELLSCHAFT** [DE/DE]; 51368 Leverkusen (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MUNNES, Marc** [DE/DE]; Am. Schimmelskämpchen 14, 40699 Erkrath (DE). **GEHRMANN, Mathias** [DE/DE]; Alte Landstr. 140, 51373 Leverkusen (DE). **WICK, Maresa** [DE/DE]; Engeldamm 62, 10179 Berlin (DE). **SCHMITZ, Gerd** [DE/DE]; Turmstr. 15a, 93161 Sinzing (DE).

(74) Common Representative: **BAYER AKTIENGESELLSCHAFT**; 51368 Leverkusen (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to the identity of the inventor (Rule 4.17(i)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: GENES AND PROTEINS FOR PREVENTION, PREDICTION, PROGNOSIS AND THERAPY OF CARDIOVASCULAR DISEASE

(57) Abstract: Genes that are differentially expressed in blood vessels of cardiovascular disease patients versus blood vessels of normal people are disclosed. The genes provide novel methods, uses and compositions for the prediction, prevention, diagnosis, prognosis and treatment of cardiovascular disease.



WO 03/031650 A2

GENES AND PROTEINS FOR PREVENTION, PREDICTION, PROGNOSIS
AND THERAPY OF CARDIOVASCULAR DISEASE

TECHNICAL FIELD OF THE INVENTION

5

The present invention relates to polynucleotide sequences and polypeptides thereof for the diagnosis and treatment of cardiovascular disease, including, but not limited to, arteriosclerosis, angina pectoris, myocardial infarction, ischemia, restenosis, and arterial inflammation. Specifically, the present invention identifies and describes
10 genes which are differentially expressed in cardiovascular disease states, relative to their expression in normal, and/or in response to manipulations relevant to cardiovascular disease (e.g. incubation of isolated macrophages in the presence of enzymatic modified LDL). In particular genes that are up- or down-regulated in macrophages of patients with inherited predisposition for arteriosclerosis are
15 disclosed. Also disclosed are methods for utilizing such genes, polynucleotides or polypeptides derived from the genes as diagnostic markers for cardiovascular disease, particularly arteriosclerosis.

Still further, the present invention provides methods for the identification and
20 therapeutic use of antibodies for treatment of cardiovascular disease. Moreover, the present invention provides methods for the diagnostic monitoring of patients undergoing clinical evaluation for the treatment of cardiovascular disease, and for monitoring the efficacy of compounds in clinical trials. Additionally, the present invention describes methods for the diagnostic evaluation and prognosis of various
25 cardiovascular diseases, and for the identification of subjects exhibiting a predisposition to such conditions

Methods of screening for activators and inhibitors which can be used for the regulation of polypeptides derived from the genes and therapeutic uses of these
30 modulators are also disclosed.

BACKGROUND OF THE INVENTION

Cardiovascular diseases such as arteriosclerosis, ischemia, myocardial infarction, and angina pectoris are a major health risk throughout the industrialized world.

5

Arteriosclerosis

The principal cell types of the artery wall, the endothelial cell, the smooth muscle cell and the monocyte/macrophage, are major players in the events involved in initiation and evolution of the arteriosclerotic plaque. The process, in normal
10 circumstances a protective response to insults to the endothelium and smooth muscle cells (SMCs) of the wall of the artery, consists of the formation of fibrofatty and fibrous lesions (fatty streaks) or plaques, preceded and accompanied by inflammation.

15

The first observable event in the formation of an arteriosclerotic plaque occurs when blood-borne monocytes adhere to the vascular endothelial layer and transmigrate through to the sub-endothelial space. Within the vessel wall monocytes differentiate into macrophages due to the extracellular stimuli. Adjacent endothelial cells at the
20 same time produce oxidized low density lipoprotein (LDL). These oxidized LDL's are then taken up in large amounts by the macrophages through scavenger receptors expressed on their surfaces. In contrast to the tightly regulated pathway by which native LDL (nLDL) is taken up by nLDL specific receptors. But not only genes of the LDL uptake machinery are of great diagnostic and therapeutic interest since the
25 cellular cholesterol content is normally under strict homeostatic control, and mechanisms of *de novo* synthesis and efflux are also highly regulated. Cholesterol efflux pathways have been a focus of much recent attention, as studies on protein and cholesterol transport converged, pointing at cholesterol-rich membrane micro-domains or proteolipid complexes, or both, as carriers of newly synthesised free
30 cholesterol to the plasma membrane. Cellular cholesterol is accrued by:

- (i) internalisation of intact low-density lipoprotein (LDL) carrying cholesteryl-ester by endocytosis via high-affinity LDL receptors;
- (ii) selective uptake of free cholesterol by monomer exchange, mainly from LDL;
- (iii) selective uptake of cholesteryl ester by exchange, mainly from HDL; and
- (iv) *de novo* synthesis of cholesterol by the mevalonate pathway in the endoplasmic reticulum (ER).

10

Several lines of evidence suggest that the pathways involved in transport of protein and cholesterol from the ER to the plasma membrane are different. In arteriosclerosis either of these pathways is disturbed and as a consequence lipid-filled macrophages, so called foam cells, and their accumulation lead to the development of fatty streaks. Some fatty streaks subsequently accumulate smooth muscle cells, which migrate from the medial layer. With the secretion of extracellular matrix molecules by the smooth muscle cells, fibrous plaques develop and increase in size. Progression of the disease is characterised by the accumulation of lipids and fibrous elements in the large arteries. The advanced lesions of arteriosclerosis may occlude the artery concerned, and result from an excessive inflammatory-fibroproliferative response to numerous different forms of insult, resulting in restriction of the flow of blood, leading to ischemia. For example, shear stresses are thought to be responsible for the frequent occurrence of arteriosclerotic plaques in regions of the circulatory system where turbulent blood flow occurs, such as branch points and irregular structures [for review see Lusis et al., (2)].

25

Especially the anterior descending branch of the left coronary artery is susceptible to arteriosclerosis. With time, these plaques can lead to a partial reduction or a sudden total block of the blood's flow. In rare cases coronary artery spasm of unknown origin can provoke that situation as well. The major complications are angina pectoris, myocardial infarction, and sudden cardiac death.

30

Ischemia

Ischemia is a sequela of arteriosclerosis characterised by a lack of oxygen supply in tissues of organs due to inadequate perfusion. Such inadequate perfusion can have
5 number of natural causes, including arterioosclerotic or restenotic lesions, anaemia, or stroke, to name a few. Many medical interventions, such as the interruption of the flow of blood during bypass surgery, for example, also lead to ischemia. In addition to sometimes being caused by diseased cardiovascular tissue, ischemia may sometimes affect cardiovascular tissue, such as in ischemic heart disease. Ischemia
10 may occur in any organ, however, that is suffering a lack of oxygen supply. Not infrequently, two or more causes of ischemia will coexist, such as an increase in oxygen demand due to left ventricular hypertrophy and a reduction in oxygen supply secondary to coronary arteriosclerosis.

Angina pectoris

Angina pectoris, another sequela of arteriosclerosis, is characterised by episodes of chest discomfort and pressure due to insufficient blood supply, typically precipitated by exertion and relieved by rest. Angina pectoris is usually triggered by activity, emotional stress, or temperatures and persists only a few minutes. The blood
20 circulation and oxygen supply of the cardiac muscle is reduced for a short period of time due to constriction of coronary arteries.

With progressive arteriosclerosis sensations of pain can be experienced even during periods of rest. Angina pectoris certainly is a sign that a person is at increased risk of
25 heart attack.

Myocardial infarction

A heart attack or myocardial infarction occurs when the supply of oxygen and
30 nutrient-rich blood to the heart muscle is severely reduced or cut off completely, resulting in sharp pain. In most patients an acute thrombus, often associated with

plaque rupture, occludes the artery. If the blood supply is shut down for a long time cardiac muscle cells die from lack of oxygen. If only a small part of the heart muscle is deprived of oxygen the victim might recover. However, disability or death can result, depending on how much the heart muscle is damaged. Therefore, people with
5 a genetic predisposition or risk factors like diabetes, hypertension, high cholesterol, and obesity should be extremely careful.

Early diagnosis of patients at risk to develop arteriosclerosis will allow to initiate early preventative steps. Prevention, optimal treatment, and rehabilitation measures
10 are necessary to avoid the sequela of arteriosclerosis such as stroke, angina pectoris, ischemia, or myocardial infarction, to improve the quality of life and to extend overall survival in these patients.

Arteriosclerosis, the most prevalent cardiovascular disease, is the principal cause of
15 heart attack, stroke, and gangrene of the extremities, and thereby the principle cause of death in the United States. Arteriosclerosis is now recognized as a multifactorial disease process associated with several important environmental and genetic risk factors [for a detailed review, see Ross et al. (1)]. Such risk factors include hyper-
20 tension, elevated levels of homocysteine or LDL/VLDL, smoking, diabetes mellitus, and obesity. Because of the presumed role of the excessive inflammatory-fibroproliferative response in arteriosclerosis and ischemia, a number of researchers have investigated, in the context of arterial injury, the expression of certain factors involved in inflammation, cell recruitment and proliferation. These factors include
25 growth factors, cytokines, and other chemicals, including lipids involved in cell recruitment and migration, cell proliferation and the control of lipid and protein synthesis. These results so far have not lead to satisfactory improvements for the patients and subsequently there is an ongoing need for novel preventive, predictive, diagnostic, prognostic and therapeutic compositions, uses and methods. The
30 foregoing studies are aimed at defining the role of particular gene products in the excessive inflammatory-fibroproliferative response leading to arteriosclerotic plaque formation.

SUMMARY OF THE INVENTION

5 The present invention relates to novel preventive, predictive, diagnostic, prognostic and therapeutic compositions, uses and methods for cardiovascular diseases and arteriosclerosis in particular. Specifically, 74 genes are identified and described which are differentially expressed in cardiovascular disease states, relative to their expression in normal, or non-cardiovascular disease states, as well as derivatives, fragments, analogues and homologues thereof. Especially membrane bound marker
10 gene products containing extracellular domains can be a particularly useful target for treatment methods as well as diagnostic and clinical monitoring methods.

The invention is based, in part, on systematic search strategies involving *in vivo and in vitro* cardiovascular disease experiments coupled with sensitive and high
15 throughput gene expression assays, based on DNA chip technology. In contrast to approaches that merely evaluate the expression of a given gene product presumed to play a role in a disease process, the search strategies and assays used herein permit the identification of all genes, whether known or novel, that are expressed or repressed in the disease condition, as well as the evaluation of their temporal
20 regulation and function during disease progression. This comprehensive approach and evaluation permits the discovery of novel genes and gene products, as well as the identification of an array of genes and gene products (whether novel or known) involved in novel pathways that play a major role in the disease pathology. Thus based on the identification of genes relevant for the pathophysiology of
25 cardiovascular diseases such as arteriosclerosis and it's sequela, the invention provides novel targets useful for prevention, prediction, diagnosis, prognosis monitoring, rational drug screening and design, and/or other therapeutic intervention of cardiovascular diseases and arteriosclerosis in particular.

30 "Differential expression", as used herein, refers to both quantitative as well as qualitative differences in the genes' expression patterns depending on differential

- 7 -

development and/or reaction to lipid environment of macrophages. Differentially expressed genes may represent "marker genes," and/or "target genes" which are named "CVD genes" or "CVD gene" hereinafter. "CVD genes" or "CVD gene" refers to polynucleotides but also to the polypeptides encoded thereby. The expression pattern of a differentially expressed "CVD gene" may be utilized as part of a prognostic or diagnostic cardiovascular disease evaluation. Alternatively, a "CVD gene" may be used in methods for identifying reagents and compounds and uses of these reagents and compounds for the treatment of cardiovascular disease as well as methods of treatment. Also "CVD gene" refers to a differentially expressed gene involved in cardiovascular diseases such that modulation of the level of target gene expression or of target gene product activity may act to ameliorate a cardiovascular disease condition. Compounds that modulate target gene expression or activity of the target gene product can be used in the treatment of cardiovascular disease.

It is an objective of the invention to provide methods and reagents for the prediction, prevention, diagnosis, prognosis and therapy of cardiovascular disease and in particular arteriosclerosis.

In one embodiment, the invention pertains to a method of determining the phenotype of a cell or tissue, comprising detecting the differential expression, relative to a normal or untreated cell, of at least one nucleic acid comprising SEQ ID Nos. 1 to 74, wherein the nucleic acid is differentially expressed by at least about 1.5 fold, at least about 2 fold, at least about 3 fold.

In a further aspect the invention pertains to a method of determining the phenotype of a cell or tissue, comprising detecting the differential expression, relative to a normal or untreated cell, of at least one nucleic acid which hybridises under stringent conditions to one of SEQ ID Nos. 1 to 74, wherein the nucleic acid is differentially expressed by at least at least about 1.5 fold, at least about 2 fold or at least about 3 fold.

In another embodiment of the invention a "CVD gene" or a gene product of a "CVD gene" can be used to identify cells or tissue in individuals which exhibit a phenotype predisposed to cardiovascular disease or a diseased phenotype, thereby (a) predicting whether an individual is at risk for the development, or (b) diagnosing whether an individual is having, or (c) prognosing the progression or the outcome of the treatment cardiovascular disease and arteriosclerosis in particular.

In yet another embodiment the invention provides methods of screening for agents which regulate the activity of a polypeptide encoded by a "CVD gene". A test compound is contacted with a polypeptide encoded by a "CVD gene". Binding of the test compound to the polypeptide is detected. A test compound which binds to the polypeptide is thereby identified as a potential therapeutic agent for the treatment of cardiovascular disease and more particularly arteriosclerosis.

In even another embodiment the invention provides another method of screening for agents which regulate the activity of a polypeptide encoded by a "CVD gene". A test compound is contacted with a polypeptide encoded by a "CVD gene". A biological activity mediated by the polypeptide is detected. A test compound which decreases the biological activity is thereby identified as a potential therapeutic agent for decreasing the activity of the polypeptide encoded by a "CVD gene" in cardiovascular disease and arteriosclerosis in particular. A test compound which increases the biological activity is thereby identified as a potential therapeutic agent for increasing the activity of the polypeptide encoded by a "CVD gene" in cardiovascular disease and arteriosclerosis in particular.

In another embodiment the invention provides a method of screening for agents which regulate the activity of a "CVD gene". A test compound is contacted with a "CVD gene" polynucleotide. Binding of the test compound to the "CVD gene" polynucleotide is detected. A test compound which binds to the polynucleotide is thereby identified as a potential therapeutic agent for regulating the activity of the "CVD gene" in cardiovascular disease and arteriosclerosis in particular.

The invention thus provides "CVD genes" which can be used to identify compounds which may act, for example, as regulators or modulators such as agonists and antagonists, partial agonists, inverse agonists, activators, co-activators and inhibitors of the polypeptide encoded by a "CVD gene". Accordingly, the invention provides reagents and methods for regulating a "CVD gene" polynucleotide or a polypeptide encoded by a "CVD gene" in cardiovascular disease and more particularly arteriosclerosis. The regulation can be an up- or down regulation. Reagents that modulate the expression, stability or amount of a "CVD gene" polynucleotide or the activity of the polypeptide encoded by a "CVD gene" can be a protein, a peptide, a peptidomimetic, a nucleic acid, a nucleic acid analogue (e.g. peptide nucleic acid, locked nucleic acid) or a small molecule.. Methods that modulate the expression, stability or amount of a "CVD gene" polynucleotide or the activity of the polypeptide encoded by a "CVD gene" can be gene replacement therapies, antisense, ribozyme and triplex nucleic acid approaches.

In one embodiment of the invention provides antibodies which specifically bind to a full-length or partial "CVD gene" polynucleotide or a polypeptide for use in prediction, prevention, diagnosis, prognosis and treatment of cardiovascular disease.

Yet another embodiment of the invention is the use of a reagent which specifically binds to a "CVD gene" polynucleotide or a polypeptide encoded by a "CVD gene" in the preparation of a medicament for the treatment of cardiovascular disease and arteriosclerosis in particular.

Still another embodiment is the use of a reagent that modulates the activity or stability of a "CVD gene" polypeptide or the expression, amount or stability of a "CVD gene" mRNA in the preparation of a medicament for the treatment of cardiovascular disease and arteriosclerosis in particular.

30

Still another embodiment of the invention is a pharmaceutical composition which includes a reagent which specifically binds to a "CVD gene" polynucleotide or a polypeptide encoded by a "CVD gene", and a pharmaceutically acceptable carrier.

- 5 Yet another embodiment of the invention is a pharmaceutical composition including the subject nucleic acids. In one embodiment, a reagent which alters the level of expression in a cell of a nucleic acid comprising one of SEQ ID Nos. 1 to 74, or a sequence complementary thereto, is identified by providing a cell, treating the cell with a test reagent, determining the level of expression in the cell of a nucleic acid of
- 10 SEQ ID Nos. 1 to 74 or a sequence complementary thereto, and comparing the level of expression of the nucleic acid in the treated cell with the level of expression of the nucleic acid in an untreated cell, wherein a change in the level of expression of the nucleic acid in the treated cell relative to the level of expression of the nucleic acid in the untreated cell is indicative of an agent which alters the level of expression of the
- 15 nucleic acid in a cell. The invention further provides a pharmaceutical composition comprising a reagent identified by this method.

- Another embodiment of the invention is a pharmaceutical composition which includes a polypeptide either encoded by a nucleic acid having a nucleotide sequence
- 20 comprising one of SEQ ID Nos. 1 to 74 or a sequence complementary thereto, or having the sequence of SEQ ID Nos. 75 to 147. In one embodiment, the invention pertains to a pharmaceutical composition comprising a nucleic acid including a sequence which hybridises under stringent conditions to one of SEQ ID Nos. 1 to 74 or a sequence complementary thereto. Pharmaceutical compositions, useful in the
- 25 present invention may further include fusion proteins comprising the amino acid sequence of SEQ ID Nos. 75 to 147, or a fragment thereof, antibodies, or antibody fragments

DETAILED DESCRIPTION OF THE INVENTION

Definitions

5 “Biological activity” or “bioactivity” or “activity” or “biological function”, which are used interchangeably, herein mean an effector or antigenic function that is directly or indirectly performed by a polypeptide (whether in its native or denatured conformation), or by any fragment thereof *in vivo* or *in vitro*. Biological activities include but are not limited to binding to polypeptides, binding to other proteins or molecules, enzymatic activity, signal transduction, activity as a DNA binding
10 protein, as a transcription regulator, ability to bind damaged DNA, etc. A bioactivity can be modulated by directly affecting the subject polypeptide. Alternatively, a bioactivity can be altered by modulating the level of the polypeptide, such as by modulating expression of the corresponding gene.

15 The term “biomarker” refers a biological molecule, e.g., a nucleic acid, peptide, hormone, etc., whose presence or concentration can be detected and correlated with a known condition, such as a disease state.

The term “biological sample”, as used herein, refers to a sample obtained from an
20 organism or from components (e.g., cells) of an organism. The sample may be of any biological tissue or fluid. Frequently the sample will be a “clinical sample” which is a sample derived from a patient. Such samples include, but are not limited to, sputum, blood, blood cells (e.g., white cells), tissue or fine needle biopsy samples, urine, peritoneal fluid, and pleural fluid, or cells therefrom. Biological samples may
25 also include sections of tissues such as frozen sections taken for histological purposes.

By “array” or “matrix” is meant an arrangement of addressable locations or
“addresses” on a device. The locations can be arranged in two dimensional arrays,
30 three dimensional arrays, or other matrix formats. The number of locations can range from several to at least hundreds of thousands. Most importantly, each location

represents a totally independent reaction site. Arrays include but are not limited to nucleic acid arrays, protein arrays and antibody arrays. A "nucleic acid array" refers to an array containing nucleic acid probes, such as oligonucleotides or larger portions of genes. The nucleic acid on the array is preferably single stranded. Arrays wherein the probes are oligonucleotides are referred to as "oligonucleotide arrays" or "oligonucleotide chips." A "microarray," also referred to herein as a "biochip" or "biological chip" is an array of regions having a density of discrete regions of at least about 100/cm², and preferably at least about 1000/cm². The regions in a microarray have typical dimensions, e.g., diameters, in the range of between about 10-250 μm, and are separated from other regions in the array by about the same distance. A "protein array" refers to an array containing polypeptide probes or protein probes which can be in native form or denatured. An "antibody array" refers to an array containing antibodies which include but are not limited to monoclonal antibodies (e.g. from a mouse), chimeric antibodies, humanized antibodies or phage antibodies and single chain antibodies as well as fragments from antibodies.

"Small molecule" as used herein, is meant to refer to a composition, which has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic (carbon-containing) or inorganic molecules. Many pharmaceutical companies have extensive libraries of chemical and/or biological mixtures, often fungal, bacterial, or algal extracts, which can be screened with any of the assays of the invention to identify compounds that modulate a bioactivity.

"Marker gene," as used herein, refers to a differentially expressed gene whose expression pattern may be utilized as part of a prognostic or diagnostic cardiovascular disease evaluation, or which, alternatively, may be used in methods for identifying compounds useful for the treatment of cardiovascular disease. A marker gene may also have the characteristics of a target gene.

5 "Target gene", as used herein, refers to a differentially expressed gene involved in cardiovascular disease in a manner by which modulation of the level of target gene expression or of target gene product activity may act to ameliorate symptoms of cardiovascular disease. A target gene may also have the characteristics of a marker gene.

10 The terms "modulated" or "modulation" and "differentially regulated" as used herein refer to both upregulation (i.e., activation or stimulation (e.g., by agonizing or potentiating) and down regulation [i.e., inhibition or suppression (e.g., by antagonizing, decreasing or inhibiting)].

15 "Transcriptional regulatory unit" refers to DNA sequences, such as initiation signals, enhancers, and promoters, which induce or control transcription of protein coding sequences with which they are operably linked. In preferred embodiments, transcription of one of the genes is under the control of a promoter sequence (or other transcriptional regulatory sequence) which controls the expression of the recombinant gene in a cell-type in which expression is intended. It will also be understood that the recombinant gene can be under the control of transcriptional regulatory sequences which are the same or which are different from those sequences
20 which control transcription of the naturally occurring forms of the polypeptide.

The term "derivative" refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, or amino group.
25 A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

30

The present invention provides nucleic acid sequences and proteins encoded thereby, as well as probes derived from the nucleic acid sequences, antibodies directed to the encoded proteins, and predictive, preventive, diagnostic, prognostic and therapeutic methods for individuals which are at risk for or which have cardiovascular disease and arteriosclerosis in particular. The sequences disclosure herein have been found to be differentially expressed in samples relevant for cardiovascular diseases.

The present invention is based on the identification of 74 genes that are differentially regulated (up- or downregulated) in macrophages with/without incubation with eLDL of patients with clinical evidence of CVD. The identification of 74 human genes which were not known to be differentially regulated in cardiovascular disease states and their significance for the disease is described in the working examples herein. The characterisation of the expression of these genes in particular disease states provides newly identified roles in cardiovascular diseases. The gene names, the database accession numbers (GenBank and UniGene) and the fold-regulation values are given in the Tables 1 and 2. The primer sequences used for the gene amplification are shown in Table 3. Table 4 provides information about the gene function the functional class of the proteins which are encoded by the 74 differentially regulated genes.

In either situation, detecting expression of these genes in excess of normal expression provides for the diagnosis of cardiovascular disease. Furthermore, in testing the efficacy of compounds during clinical trials, a decrease in the level of the expression of these genes corresponds to a return from a disease condition to a normal state, and thereby indicates a positive effect of the compound. The cardiovascular diseases that may be so diagnosed, monitored in clinical trials, and treated include but are not limited to arteriosclerosis, ischemia, restenosis, and arterial inflammation.

The examples presented below, demonstrate the use of the cardiovascular disease experiments of the invention to identify cardiovascular disease target genes, and

demonstrates the use of marker genes in diagnostics and as surrogate markers for testing the efficacy of candidate drugs in basic research and in clinical trials.

5 “Gene or Genes” as used herein refers to the polynucleotides of SEQ ID NO. 1 to 74, as well as derivatives, fragments, analogs and homologues thereof, the polypeptides encoded thereby, the polypeptides of SEQ ID NO. 75 to 147 and the corresponding genomic transcription units which can be derived or identified with standard techniques well known in the art using the information disclosed in Tables 1 to 3. The GenBank and the UniGene accession numbers of the polynucleotide sequences
10 of the SEQ IDs NO. 1 to 74 are shown in the Tables 1 and 2.

The invention further relates to the use of:

- 15 a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
- b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 20 c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 25 d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c);
- 30 e) an antisense molecule targeting one of the polynucleotide sequences specified in (a) to (d);

- f) a purified polypeptide encoded by a polynucleotide sequence specified in (a) to (d)
- g) a purified polypeptide comprising at least one of the sequences of SEQ ID NO. 75 to 147;
- h) an antibody capable of binding to one of the polynucleotide specified in (a) to (d) or a polypeptide specified in (f) and (g)
- i) a reagent identified by any of the methods as specified below that modulates the amount or activity of a polynucleotide sequence specified in (a) to (d) or a polypeptide specified in (f) and (g)

for the preparation of compositions for the prevention, prediction, diagnosis, prognosis or a medicament for the treatment of a cardiovascular disease.

Polynucleotides

A „CVD gene“ polynucleotide can be single- or double-stranded and comprises a coding sequence or the complement of a coding sequence for a „CVD gene“ polypeptide. Degenerate nucleotide sequences encoding human „CVD gene“ polypeptides, as well as homologous nucleotide sequences which are at least about 50, 55, 60, 65, 70, preferably about 75, 90, 96, or 98% identical to the nucleotide sequences of SEQ ID NO.1 to 74 also are „CVD gene“ polynucleotides. Percent sequence identity between the sequences of two polynucleotides is determined using computer programs such as ALIGN which employ the FASTA algorithm, using an affine gap search with a gap open penalty of -12 and a gap extension penalty of -2. Complementary DNA (cDNA) molecules, species homologues, and variants of „CVD gene“ polynucleotides which encode biologically active „CVD gene“ polypeptides also are „CVD gene“ polynucleotides.

Preparation of Polynucleotides

5 A naturally occurring „CVD gene“ polynucleotide can be isolated free of other cellular components such as membrane components, proteins, and lipids. Polynucleotides can be made by a cell and isolated using standard nucleic acid purification techniques, or synthesized using an amplification technique, such as the polymerase chain reaction (PCR), or by using an automatic synthesizer. Methods for isolating polynucleotides are routine and are known in the art. Any such technique for obtaining a polynucleotide can be used to obtain isolated „CVD gene“ polynucleotides. For example, restriction enzymes and probes can be used to isolate polynucleotide fragments which comprises „CVD gene“ nucleotide sequences. Isolated polynucleotides are in preparations which are free or at least 70, 80, or 90% free of other molecules.

15 „CVD gene“ cDNA molecules can be made with standard molecular biology techniques, using „CVD gene“ mRNA as a template. Any RNA isolation technique which does not select against the isolation of mRNA may be utilized for the purification of such RNA samples. See, for example, Sambrook et al., (3).; and Ausubel, F. M. et al.,(4) , both of which are incorporated herein by reference in their entirety. Additionally, large numbers of tissue samples may readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski, P. (1989, U.S. Pat. No. 4,843,155), which is incorporated herein by reference in its entirety.

25 „CVD gene“ cDNA molecules can thereafter be replicated using molecular biology techniques known in the art and disclosed in manuals such as Sambrook et al., (3) . An amplification technique, such as PCR, can be used to obtain additional copies of polynucleotides of the invention, using either human genomic DNA or cDNA as a template.

30

Alternatively, synthetic chemistry techniques can be used to synthesize „CVD gene“ polynucleotides. The degeneracy of the genetic code allows alternate nucleotide sequences to be synthesized which will encode a „CVD gene“ polypeptide or a biologically active variant thereof.

5

Identification of differential expression

Transcripts within the collected RNA samples which represent RNA produced by differentially expressed genes may be identified by utilizing a variety of methods which are well known to those of skill in the art. For example, differential screening [Tedder, T. F. et al., (5)], subtractive hybridization [Hedrick, S. M. et al., (6); Lee, S. W. et al., (7)], and, preferably, differential display (Liang, P., and Pardee, A. B., 1993, U.S. Pat. No. 5,262,311, which is incorporated herein by reference in its entirety), may be utilized to identify nucleic acid sequences derived from genes that are differentially expressed.

15

Differential screening involves the duplicate screening of a cDNA library in which one copy of the library is screened with a total cell cDNA probe corresponding to the mRNA population of one cell type while a duplicate copy of the cDNA library is screened with a total cDNA probe corresponding to the mRNA population of a second cell type. For example, one cDNA probe may correspond to a total cell cDNA probe of a cell type derived from a control subject, while the second cDNA probe may correspond to a total cell cDNA probe of the same cell type derived from an experimental subject. Those clones which hybridize to one probe but not to the other potentially represent clones derived from genes differentially expressed in the cell type of interest in control versus experimental subjects.

20

25

Subtractive hybridization techniques generally involve the isolation of mRNA taken from two different sources, e.g., control and experimental tissue, the hybridization of the mRNA or single-stranded cDNA reverse-transcribed from the isolated mRNA, and the removal of all hybridized, and therefore double-stranded, sequences. The

30

remaining non-hybridized, single-stranded cDNAs, potentially represent clones derived from genes that are differentially expressed in the two mRNA sources. Such single-stranded cDNAs are then used as the starting material for the construction of a library comprising clones derived from differentially expressed genes.

5

The differential display technique describes a procedure, utilizing the well known polymerase chain reaction (PCR; the experimental embodiment set forth in Mullis, K. B., 1987, U.S. Pat. No. 4,683,202) which allows for the identification of sequences derived from genes which are differentially expressed. First, isolated RNA
10 is reverse-transcribed into single-stranded cDNA, utilizing standard techniques which are well known to those of skill in the art. Primers for the reverse transcriptase reaction may include, but are not limited to, oligo dT-containing primers, preferably of the reverse primer type of oligonucleotide described below. Next, this technique uses pairs of PCR primers, as described below, which allow for the amplification of
15 clones representing a random subset of the RNA transcripts present within any given cell. Utilizing different pairs of primers allows each of the mRNA transcripts present in a cell to be amplified. Among such amplified transcripts may be identified those which have been produced from differentially expressed genes.

20 The reverse oligonucleotide primer of the primer pairs may contain an oligo dT stretch of nucleotides, preferably eleven nucleotides long, at its 5' end, which hybridises to the poly(A) tail of mRNA or to the complement of a cDNA reverse transcribed from an mRNA poly(A) tail. Second, in order to increase the specificity of the reverse primer, the primer may contain one or more, preferably two, additional
25 nucleotides at its 3' end. Because, statistically, only a subset of the mRNA derived sequences present in the sample of interest will hybridise to such primers, the additional nucleotides allow the primers to amplify only a subset of the mRNA derived sequences present in the sample of interest. This is preferred in that it allows more accurate and complete visualization and characterization of each of the bands
30 representing amplified sequences.

The forward primer may contain a nucleotide sequence expected, statistically, to have the ability to hybridise to cDNA sequences derived from the tissues of interest. The nucleotide sequence may be an arbitrary one, and the length of the forward oligonucleotide primer may range from about 9 to about 13 nucleotides, with about 10 nucleotides being preferred. Arbitrary primer sequences cause the lengths of the amplified partial cDNAs produced to be variable, thus allowing different clones to be separated by using standard denaturing sequencing gel electrophoresis. PCR reaction conditions should be chosen which optimise amplified product yield and specificity, and, additionally, produce amplified products of lengths which may be resolved utilizing standard gel electrophoresis techniques. Such reaction conditions are well known to those of skill in the art, and important reaction parameters include, for example, length and nucleotide sequence of oligonucleotide primers as discussed above, and annealing and elongation step temperatures and reaction times. The pattern of clones resulting from the reverse transcription and amplification of the mRNA of two different cell types is displayed via sequencing gel electrophoresis and compared. Differences in the two banding patterns indicate potentially differentially expressed genes.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. Randomly-primed libraries are preferable, in that they will contain more sequences which contain the 5' regions of genes. Use of a randomly primed library may be especially preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries can be useful for extension of sequence into 5' nontranscribed regulatory regions.

Commercially available capillary electrophoresis systems can be used to analyse the size or confirm the nucleotide sequence of PCR or sequencing products. For example, capillary sequencing can employ flowable polymers for electrophoretic separation, four different fluorescent dyes (one for each nucleotide) which are laser activated, and detection of the emitted wavelengths by a charge coupled device camera. Output/light intensity can be converted to electrical signal using appropriate

software (e.g. GENOTYPER and Sequence NAVIGATOR, Perkin Elmer; ABI), and the entire process from loading of samples to computer analysis and electronic data display can be computer controlled. Capillary electrophoresis is especially preferable for the sequencing of small pieces of DNA which might be present in limited amounts in a particular sample.

Once potentially differentially expressed gene sequences have been identified via bulk techniques such as, for example, those described above, the differential expression of such putatively differentially expressed genes should be corroborated. Corroboration may be accomplished via, for example, such well known techniques as Northern analysis and/or RT-PCR. Upon corroboration, the differentially expressed genes may be further characterized, and may be identified as target and/or marker genes, as discussed, below.

Also, amplified sequences of differentially expressed genes obtained through, for example, differential display may be used to isolate full length clones of the corresponding gene. The full length coding portion of the gene may readily be isolated, without undue experimentation, by molecular biological techniques well known in the art. For example, the isolated differentially expressed amplified fragment may be labeled and used to screen a cDNA library. Alternatively, the labeled fragment may be used to screen a genomic library.

An analysis of the tissue distribution of the mRNA produced by the identified genes may be conducted, utilizing standard techniques well known to those of skill in the art. Such techniques may include, for example, Northern analyses and RT-PCR. Such analyses provide information as to whether the identified genes are expressed in tissues expected to contribute to cardiovascular disease. Such analyses may also provide quantitative information regarding steady state mRNA regulation, yielding data concerning which of the identified genes exhibits a high level of regulation in, preferably, tissues which may be expected to contribute to cardiovascular disease.

Such analyses may also be performed on an isolated cell population of a particular cell type derived from a given tissue. Additionally, standard in situ hybridization techniques may be utilized to provide information regarding which cells within a given tissue express the identified gene. Such analyses may provide information regarding the biological function of an identified gene relative to cardiovascular disease in instances wherein only a subset of the cells within the tissue is thought to be relevant to cardiovascular disease.

Extending Polynucleotides

In one embodiment of such a procedure for the identification and cloning of full length gene sequences, RNA may be isolated, following standard procedures, from an appropriate tissue or cellular source. A reverse transcription reaction may then be performed on the RNA using an oligonucleotide primer complimentary to the mRNA that corresponds to the amplified fragment, for the priming of first strand synthesis. Because the primer is anti-parallel to the mRNA, extension will proceed toward the 5' end of the mRNA. The resulting RNA hybrid may then be "tailed" with guanines using a standard terminal transferase reaction, the hybrid may be digested with RNAase H, and second strand synthesis may then be primed with a poly-C primer. Using the two primers, the 5' portion of the gene is amplified using PCR. Sequences obtained may then be isolated and recombined with previously isolated sequences to generate a full-length cDNA of the differentially expressed genes of the invention. For a review of cloning strategies and recombinant DNA techniques, see e.g., Sambrook et al., (3); and Ausubel et al., (4).

Various PCR-based methods can be used to extend the nucleic acid sequences disclosed herein to detect upstream sequences such as promoters and regulatory elements. For example, restriction site PCR uses universal primers to retrieve unknown sequence adjacent to a known locus [Sarkar,(8)]. Genomic DNA is first amplified in the presence of a primer to a linker sequence and a primer specific to the known region. The amplified sequences are then subjected to a second round of PCR

with the same linker primer and another specific primer internal to the first one. Products of each round of PCR are transcribed with an appropriate RNA polymerase and sequenced using reverse transcriptase.

5 Inverse PCR also can be used to amplify or extend sequences using divergent primers based on a known region [Triglia et al., (9)]. Primers can be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences Inc., Plymouth, Minn.), to be 2230 nucleotides in length, to have a GC content of 50% or more, and to anneal to the target sequence at
10 temperatures about 68-72 °C. The method uses several restriction enzymes to generate a suitable fragment in the known region of a gene. The fragment is then circularized by intramolecular ligation and used as a PCR template.

Another method which can be used is capture PCR, which involves PCR ampli-
15 fication of DNA fragments adjacent to a known sequence in human and yeast artificial chromosome DNA [Lagerstrom et al.,(10)]. In this method, multiple restriction enzyme digestions and ligations also can be used to place an engineered double-stranded sequence into an unknown fragment of the DNA molecule before performing PCR.

20 Another method which can be used to retrieve unknown sequences is that of Parker et al., (11). Additionally, PCR, nested primers, and PROMOTERFINDER libraries (CLONTECH, Palo Alto, Calif.) can be used to walk genomic DNA (CLONTECH, Palo Alto, Calif.). This process avoids the need to screen libraries and is useful in
25 finding intron/exon junctions.

The sequences of the identified genes may be used, utilizing standard techniques, to place the genes onto genetic maps, e.g., mouse [Copeland & Jenkins, (12)] and human genetic maps [Cohen, et al., (13)]. Such mapping information may yield
30 information regarding the genes' importance to human disease by, for example,

identifying genes which map near genetic regions to which known genetic cardiovascular disease tendencies map.

Identification of Polynucleotide Variants and Homologues

5

Variants and homologues of the „CVD gene“ polynucleotides described above also are „CVD gene“ polynucleotides. Typically, homologous „CVD gene“ polynucleotide sequences can be identified by hybridization of candidate polynucleotides to known „CVD gene“ polynucleotides under stringent conditions, as is known in the art. For example, using the following wash conditions: 2X SSC (0.3 M NaCl, 0.03 M sodium citrate, pH 7.0), 0.1% SDS, room temperature twice, 30 minutes each; then 10 2X SSC, 0.1% SDS, 50 EC once, 30 minutes; then 2X SSC, room temperature twice, 10 minutes each homologous sequences can be identified which contain at most about 25-30% basepair mismatches. More preferably, homologous nucleic acid strands contain 15-25% basepair mismatches, even more preferably 5-15% basepair mismatches.

Species homologues of the „CVD gene“ polynucleotides disclosed herein also can be identified by making suitable probes or primers and screening cDNA expression libraries from other species, such as mice, monkeys, or yeast. Human variants of „CVD gene“ polynucleotides can be identified, for example, by screening human cDNA expression libraries. It is well known that the T_m of a double-stranded DNA decreases by 1-1.5 °C with every 1% decrease in homology [Bonner et al., (14)]. Variants of human „CVD gene“ polynucleotides or „CVD gene“ polynucleotides of other species can therefore be identified by hybridizing a putative homologous „CVD gene“ polynucleotide with a polynucleotide having a nucleotide sequence of one of the sequences of the SEQ ID Nos:1 to 74 or the complement thereof to form a test hybrid. The melting temperature of the test hybrid is compared with the melting temperature of a hybrid comprising polynucleotides having perfectly complementary nucleotide sequences, and the number or percent of basepair mismatches within the test hybrid is calculated.

30

Nucleotide sequences which hybridize to „CVD gene“ polynucleotides or their complements following stringent hybridization and/or wash conditions also are „CVD gene“ polynucleotides. Stringent wash conditions are well known and understood in the art and are disclosed, for example, in Sambrook et al., (3). Typically, for stringent hybridization conditions a combination of temperature and salt concentration should be chosen that is approximately 12-20°C below the calculated T_m of the hybrid under study. The T_m of a hybrid between a „CVD gene“ polynucleotide having a nucleotide sequence of one of the sequences of the SEQ ID NOS: 1 to 74 or the complement thereof and a polynucleotide sequence which is at least about 50, preferably about 75, 90, 96, or 98% identical to one of those nucleotide sequences can be calculated, for example, using the equation of Bolton and McCarthy, (15):

$$T_m = 81.5^{\circ}\text{C} - 16.6(\log_{10}[\text{Na}^+]) + 0.41(\%G + C) - 0.63(\%\text{formamide}) - 600/l,$$

where l = the length of the hybrid in basepairs.

Stringent wash conditions include, for example, 4X SSC at 65°C, or 50% formamide, 4X SSC at 28 °C, or 0.5X SSC, 0.1% SDS at 65°C. Highly stringent wash conditions include, for example, 0.2X SSC at 65°C.

The biological function of the identified genes may be more directly assessed by utilizing relevant in vivo and in vitro systems. In vivo systems may include, but are not limited to, animal systems which naturally exhibit cardiovascular disease predisposition, or ones which have been engineered to exhibit such symptoms, including but not limited to the apoE-deficient arteriosclerosis mouse model [Plump et al., (16)].

Polypeptides

“CVD gene” polypeptides according to the invention comprise an amino acid selected from the amino acid sequence which are encoded by any of the polynucleotide sequences of the SEQ ID NOS: 1 to 74 or derivatives, fragments, analogues and homologues thereof. A “CVD gene” polypeptide of the invention therefore can be a portion, a full-length, or a fusion protein comprising all or a portion of a “CVD gene” polypeptide.

10 Protein Purification

„CVD gene“ polypeptides can be purified from any cell which expresses the enzyme, including host cells which have been transfected with „CVD gene“ expression constructs. Blood vessels are an especially useful source of „CVD gene“ polypeptides. A purified „CVD gene“ polypeptide is separated from other compounds which normally associate with the „CVD gene“ polypeptide in the cell, such as certain proteins, carbohydrates, or lipids, using methods well-known in the art. Such methods include, but are not limited to, size exclusion chromatography, ammonium sulfate fractionation, ion exchange chromatography, affinity chromatography, and preparative gel electrophoresis. A preparation of purified „CVD gene“ polypeptides is at least 80% pure; preferably, the preparations are 90%, 95%, or 99% pure. Purity of the preparations can be assessed by any means known in the art, such as SDS-polyacrylamide gel electrophoresis.

25 Expression of Polynucleotides

To express a „CVD gene“ polynucleotide, the polynucleotide can be inserted into an expression vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art can be used to construct expression vectors containing sequences encoding „CVD gene“ polypeptides and appropriate transcriptional and translational

control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. Such techniques are described, for example, in Sambrook et al., (3) and in Ausubel et al., (4).

5 A variety of expression vector/host systems can be utilized to contain and express sequences encoding a „CVD gene“ polypeptide. These include, but are not limited to, microorganisms, such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression
10 vectors, insect cell systems infected with virus expression vectors (e.g., baculovirus), plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids), or animal cell systems.

The control elements or regulatory sequences are those regions of the vector
15 enhancers, promoters, 5' and 3' untranslated regions which interact with host cellular proteins to carry out transcription and translation. Such elements can vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, can be used. For example, when cloning in bacterial systems,
20 inducible promoters such as the hybrid lacZ promoter of the BLUESCRIPT phagemid (Stratagene, LaJolla, Calif.) or pSPORT1 plasmid (Life Technologies) and the like can be used. The baculovirus polyhedrin promoter can be used in insect cells. Promoters or enhancers derived from the genomes of plant cells (e.g., heat shock, RUBISCO, and storage protein genes) or from plant viruses (e.g., viral promoters or
25 leader sequences) can be cloned into the vector. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are preferable. If it is necessary to generate a cell line that contains multiple copies of a nucleotide sequence encoding a „CVD gene“ polypeptide, vectors based on SV40 or EBV can be used with an appropriate selectable marker.

30

Obtaining Polypeptides

„CVD gene“ polypeptides can be obtained, for example, by purification from human cells, by expression of „CVD gene“ polynucleotides, or by direct chemical synthesis.

5

Biologically Active Variants

„CVD gene“ polypeptide variants which are biologically active, i.e., retain an „CVD gene“ activity, also are „CVD gene“ polypeptides. Preferably, naturally or non-naturally occurring „CVD gene“ polypeptide variants have amino acid sequences which are at least about 60, 65, or 70, preferably about 75, 80, 85, 90, 92, 94, 96, or 98% identical to the amino acid sequence of any of the sequences of the SEQ ID NOS: 75 to 147 or a fragment thereof. Percent identity between a putative „CVD gene“ polypeptide variant and an amino acid sequence encoded by any of the polynucleotide sequences of the SEQ ID NOS: 75 to 147 is determined using the Needleman/Wunsch algorithm (108) with the substitutions-matrix BLOSUM62 (109) and a gap creation penalty of 8 and a gap extension penalty of 2.

10

15

20

Variations in percent identity can be due, for example, to amino acid substitutions, insertions, or deletions. Amino acid substitutions are defined as one for one amino acid replacements. They are conservative in nature when the substituted amino acid has similar structural and/or chemical properties. Examples of conservative replacements are substitution of a leucine with an isoleucine or valine, an aspartate with a glutamate, or a threonine with a serine.

25

Amino acid insertions or deletions are changes to or within an amino acid sequence. They typically fall in the range of about 1 to 5 amino acids. Guidance in determining which amino acid residues can be substituted, inserted, or deleted without abolishing biological or immunological activity of a „CVD gene“ polypeptide can be found using computer programs well known in the art, such as DNASTAR software.

30

Whether an amino acid change results in a biologically active „CVD gene“ polypeptide can readily be determined by assaying for „CVD gene“ activity, as

described for example, in the specific Examples, below. Larger insertions or deletions can also be caused by alternative splicing. Protein domains can be inserted or deleted without altering the main activity of the protein.

5 Fusion Proteins

Fusion proteins are useful for generating antibodies against „CVD gene“ polypeptide amino acid sequences and for use in various assay systems. For example, fusion proteins can be used to identify proteins which interact with portions of a „CVD
10 gene“ polypeptide. Protein affinity chromatography or library-based assays for protein-protein interactions, such as the yeast two-hybrid or phage display systems, can be used for this purpose. Such methods are well known in the art and also can be used as drug screens.

15 A „CVD gene“ polypeptide fusion protein comprises two polypeptide segments fused together by means of a peptide bond. The first polypeptide segment comprises at least 25, 50, 75, 100, 150, 200, 300, 400, 500, 600, 700 or 750 contiguous amino acids of an amino acid sequence encoded by any polynucleotide sequences of the SEQ ID NOS: 1 to 74 or of a biologically active variant, such as those described
20 above. The first polypeptide segment also can comprise full-length „CVD gene“.

The second polypeptide segment can be a full-length protein or a protein fragment. Proteins commonly used in fusion protein construction include β -galactosidase, -glucuronidase, green fluorescent protein (GFP), autofluorescent proteins, including
25 blue fluorescent protein (BFP), glutathione-S-transferase (GST), luciferase, horseradish peroxidase (HRP), and chloramphenicol acetyltransferase (CAT). Additionally, epitope tags are used in fusion protein constructions, including histidine (His) tags, FLAG tags, influenza hemagglutinin (HA) tags, Myc tags, VSV-G tags, and thioredoxin (Trx) tags. Other fusion constructions can include maltose
30 binding protein (MBP), S-tag, Lex a DNA binding domain (DBD) fusions, GAL4 DNA binding domain fusions, and herpes simplex virus (HSV) BP16 protein fusions.

A fusion protein also can be engineered to contain a cleavage site located between the „CVD gene“ polypeptide-encoding sequence and the heterologous protein sequence, so that the „CVD gene“ polypeptide can be cleaved and purified away from the heterologous moiety.

5

A fusion protein can be synthesized chemically, as is known in the art. Preferably, a fusion protein is produced by covalently linking two polypeptide segments or by standard procedures in the art of molecular biology. Recombinant DNA methods can be used to prepare fusion proteins, for example, by making a DNA construct which
10 comprises coding sequences selected from any of the polynucleotide sequences of the SEQ ID NOS:1 to in proper reading frame with nucleotides encoding the second polypeptide segment and expressing the DNA construct in a host cell, as is known in the art. Many kits for constructing fusion proteins are available from companies such as Promega Corporation (Madison, WI), Stratagene (La Jolla, CA), CLONTECH
15 (Mountain View, CA), Santa Cruz Biotechnology (Santa Cruz, CA), MBL International Corporation (MIC; Watertown, MA), and Quantum Biotechnologies (Montreal, Canada; 1-888-DNA-KITS).

Identification of Species Homologs

20

Species homologues of human a „CVD gene“ polypeptide can be obtained using „CVD gene“ polypeptide polynucleotides (described below) to make suitable probes or primers for screening cDNA expression libraries from other species, such as mice, monkeys, or yeast, identifying cDNAs which encode homologs of a „CVD gene“
25 polypeptide, and expressing the cDNAs as is known in the art.

Bacterial and Yeast Expression Systems

In bacterial systems, a number of expression vectors can be selected depending upon the use intended for the „CVD gene“ polypeptide. For example, when a large
30 quantity of the „CVD gene“ polypeptide is needed for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified

can be used. Such vectors include, but are not limited to, multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene). In a BLUESCRIPT vector, a sequence encoding the „CVD gene“ polypeptide can be ligated into the vector in frame with sequences for the amino terminal Met and the subsequent 7 residues of β -galactosidase so that a hybrid protein is produced. pIN vectors [Van Heeke & Schuster, (17)] or pGEX vectors (Promega, Madison, Wis.) also can be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems can be designed to include heparin, thrombin, or factor Xa protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH can be used. For reviews, see Ausubel et al., (4) and Grant et al., (18).

Plant and Insect Expression Systems

If plant expression vectors are used, the expression of sequences encoding „CVD gene“ polypeptides can be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV can be used alone or in combination with the omega leader sequence from TMV [Takamatsu, (19)]. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters can be used [Coruzzi et al., (19); Broglie et al., (21); Winter et al., (22)]. These constructs can be introduced into plant cells by direct DNA transformation or by pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (e.g., Hobbs or Murray, in MCGRAW HILL YEARBOOK OF SCIENCE AND TECHNOLOGY, (23)).

An insect system also can be used to express a „CVD gene“ polypeptide. For example, in one such system *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. Sequences encoding „CVD gene“ polypeptides can be
5 cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of „CVD gene“ polypeptides will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses can then be used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which „CVD gene“ polypeptides can be
10 expressed [Engelhard et al., (24)].

Mammalian Expression Systems

A number of viral-based expression systems can be used to express „CVD gene“
15 polypeptides in mammalian host cells. For example, if an adenovirus is used as an expression vector, sequences encoding „CVD gene“ polypeptides can be ligated into an adenovirus transcription/translation complex comprising the late promoter and tripartite leader sequence. Insertion in a nonessential E1 or E3 region of the viral genome can be used to obtain a viable virus which is capable of expressing a „CVD
20 gene“ polypeptide in infected host cells [Logan & Shenk, (25)]. If desired, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, can be used to increase expression in mammalian host cells.

Human artificial chromosomes (HACs) also can be used to deliver larger fragments
25 of DNA than can be contained and expressed in a plasmid. HACs of 6M to 10M are constructed and delivered to cells via conventional delivery methods (e.g., liposomes, polycationic amino polymers, or vesicles).

Specific initiation signals also can be used to achieve more efficient translation of
30 sequences encoding „CVD gene“ polypeptides. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding a „CVD

gene“ polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals (including the ATG initiation codon) should be provided. The initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons can be of various origins, both natural and synthetic. The efficiency of expression can be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used [Scharf et al., (26)].

Host Cells

A host cell strain can be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed „CVD gene“ polypeptide in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Posttranslational processing which cleaves a "prepro" form of the polypeptide also can be used to facilitate correct insertion, folding and/or function. Different host cells which have specific cellular machinery and characteristic mechanisms for Post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38), are available from the American Type Culture Collection (ATCC; 10801 University Boulevard, Manassas, VA 20110-2209) and can be chosen to ensure the correct modification and processing of the foreign protein.

Stable expression is preferred for long-term, high-yield production of recombinant proteins. For example, cell lines which stably express „CVD gene“ polypeptides can be transformed using expression vectors which can contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells can be allowed to grow for 12 days in an enriched medium before they are switched to a

selective medium. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which successfully express the introduced „CVD gene“ sequences. Resistant clones of stably transformed cells can be proliferated using tissue culture techniques appropriate to the cell type. See, for example, R.I. Freshney, (27).

Any number of selection systems can be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler et al., (28)) and adenine phosphoribosyltransferase [Lowy et al., (29)] genes which can be employed in tk⁻ or aprt⁻ cells, respectively. Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, dhfr confers resistance to methotrexate [Wigler et al., (30)], npt confers resistance to the aminoglycosides, neomycin and G418 [Colbere-Garapin et al., (31)], and als and pat confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. Additional selectable genes have been described. For example, trpB allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine [Hartman & Mulligan, (32)]. Visible markers such as anthocyanins, β -glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, can be used to identify transformants and to quantify the amount of transient or stable protein expression attributable to a specific vector system [Rhodes et al., (33)].

Detecting Expression and gene product

Although the presence of marker gene expression suggests that the „CVD gene“ polynucleotide is also present, its presence and expression may need to be confirmed. For example, if a sequence encoding a „CVD gene“ polypeptide is inserted within a marker gene sequence, transformed cells containing sequences which encode a „CVD gene“ polypeptide can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding a „CVD gene“ polypeptide under the control of a single promoter. Expression of the

marker gene in response to induction or selection usually indicates expression of the „CVD gene“ polynucleotide.

Alternatively, host cells which contain a „CVD gene“ polynucleotide and which
5 express a „CVD gene“ polypeptide can be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridization and protein bioassay or immunoassay techniques which include membrane, solution, or chip-based technologies for the detection and/or quantification of nucleic acid or protein. For example, the presence
10 of a polynucleotide sequence encoding a „CVD gene“ polypeptide can be detected by DNA-DNA or DNA-RNA hybridization or amplification using probes or fragments or fragments of polynucleotides encoding a „CVD gene“ polypeptide. Nucleic acid amplification-based assays involve the use of oligonucleotides selected from sequences encoding a „CVD gene“ polypeptide to detect transformants which
15 contain a „CVD gene“ polynucleotide.

A variety of protocols for detecting and measuring the expression of a „CVD gene“ polypeptide, using either polyclonal or monoclonal antibodies specific for the polypeptide, are known in the art. Examples include enzyme-linked immunosorbent
20 assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay using monoclonal antibodies reactive to two non-interfering epitopes on a „CVD gene“ polypeptide can be used, or a competitive binding assay can be employed. These and other assays are described in Hampton et al., (34) and Maddox et al., (35).

25 A wide variety of labels and conjugation techniques are known by those skilled in the art and can be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding „CVD gene“ polypeptides include oligo labeling, nick
30 translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, sequences encoding a „CVD gene“ polypeptide can be cloned into a

vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and can be used to synthesise RNA probes in vitro by addition of labelled nucleotides and an appropriate RNA polymerase such as T7, T3, or SP6. These procedures can be conducted using a variety of commercially available kits (Amersham Pharmacia Biotech, Promega, and US Biochemical). Suitable reporter molecules or labels which can be used for ease of detection include radio-nuclides, enzymes, and fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

10 Expression and Purification of Polypeptides

Host cells transformed with nucleotide sequences encoding a „CVD gene“ polypeptide can be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The polypeptide produced by a transformed cell can be secreted or stored intracellular depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode „CVD gene“ polypeptides can be designed to contain signal sequences which direct secretion of soluble „CVD gene“ polypeptides through a prokaryotic or eukaryotic cell membrane or which direct the membrane insertion of membrane-bound „CVD gene“ polypeptide.

As discussed above, other constructions can be used to join a sequence encoding a „CVD gene“ polypeptide to a nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). Inclusion of cleavable linker sequences such as those specific for Factor Xa or enterokinase (Invitrogen, San Diego, CA) between the purification domain and the „CVD gene“ polypeptide also can be used to facilitate purification.

One such expression vector provides for expression of a fusion protein containing a „CVD gene“ polypeptide and 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification by IMAC (immobilized metal ion affinity chromatography, as described in Porath et al., (36),
5 while the enterokinase cleavage site provides a means for purifying the „CVD gene“ polypeptide from the fusion protein. Vectors which contain fusion proteins are disclosed in Kroll et al., (37).

Chemical Synthesis

10

Sequences encoding a „CVD gene“ polypeptide can be synthesised, in whole or in part, using chemical methods well known in the art (see Caruthers et al., (38) and Horn et al., (39). Alternatively, a „CVD gene“ polypeptide itself can be produced using chemical methods to synthesise its amino acid sequence, such as by direct
15 peptide synthesis using solid-phase techniques [Merrifield, (40) and Roberge et al., (41)]. Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Optionally, fragments of „CVD gene“ polypeptides can be separately synthesized and combined using chemical methods to
20 produce a full-length molecule.

The newly synthesized peptide can be substantially purified by preparative high performance liquid chromatography [Creighton, (42)]. The composition of a synthetic „CVD gene“ polypeptide can be confirmed by amino acid analysis or
25 sequencing (e.g., the Edman degradation procedure; see Creighton, (42). Additionally, any portion of the amino acid sequence of the „CVD gene“ polypeptide can be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins to produce a variant polypeptide or a fusion protein.

Production of Altered Polypeptides

As will be understood by those of skill in the art, it may be advantageous to produce „CVD gene“ polypeptide-encoding nucleotide sequences possessing non-natural occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce an RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

The nucleotide sequences disclosed herein can be engineered using methods generally known in the art to alter „CVD gene“ polypeptide-encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the polypeptide or mRNA product. DNA shuffling by random fragmentation and PCR re-assembly of gene fragments and synthetic oligonucleotides can be used to engineer the nucleotide sequences. For example, site-directed mutagenesis can be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, introduce mutations, and so forth.

Diagnostic and Prognostic Assays

The present invention provides method for determining whether a subject is at risk for developing cardiovascular disease and arteriosclerosis in particular by detecting the disclosed biomarkers, i.e., the disclosed polynucleotide markers comprising any of the polynucleotides sequences of the SEQ ID NOS:1 to 74 and/or the polypeptide markers encoded thereby or comprising any of the polypeptide sequences of the SEQ ID NOS: 75 to 147 for cardiovascular disease and arteriosclerosis in particular in particular encoded thereby.

In clinical applications, biological samples can be screened for the presence and/or absence of the biomarkers identified herein. Such samples are for example needle

biopsy cores, surgical resection samples, or body fluids like serum and urine. For example, these methods include obtaining a biopsy, which is optionally fractionated by cryostat sectioning to enrich diseased cells to about 80% of the total cell population. In certain embodiments, nucleic acids extracted from these samples may be amplified using techniques well known in the art. The expression levels of selected markers detected would be compared with statistically valid groups of diseased and healthy samples.

In one embodiment the diagnostic method comprises determining whether a subject has an abnormal mRNA and/or protein level of the disclosed markers, such as by Northern blot analysis, reverse transcription-polymerase chain reaction (RT-PCR), in situ hybridization, immunoprecipitation, Western blot hybridization, or immunohistochemistry. According to the method, cells are obtained from a subject and the levels of the disclosed biomarkers, protein or mRNA level, is determined and compared to the level of these markers in a healthy subject. An abnormal level of the biomarker polypeptide or mRNA levels is likely to be indicative of cardiovascular disease such as arteriosclerosis.

1. Polynucleotide detection

20

In one embodiment, the method for the diagnosis or prognosis of cardiovascular disease is done by the detection of:

- (a) polynucleotide selected from the polynucleotides of the SEQ ID NOS: 1 to 74;
- (b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- (c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes

a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

- (d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c);

5

in a biological sample comprising the following steps: hybridizing any polynucleotide specified in (a) to (d) to a nucleic acid material of a biological sample, thereby forming a hybridization complex; and detecting said hybridization complex.

10

In another embodiment the method for the diagnosis or prognosis of cardiovascular disease is done as just described but, wherein before hybridization, the nucleic acid material of the biological sample is amplified.

15

In another embodiment the method for the diagnosis or prognosis of cardiovascular disease is done by the detection of:

- (a) a polynucleotide selected from the polynucleotides of the SEQ ID NOS: 1 to 74;

20

- (b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

25

- (c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- (d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c);
- (e) a polypeptide encoded by a polynucleotide sequence specified in (a) to (d)

comprising the steps of contacting a biological sample with a reagent which specifically interacts with the polynucleotide specified in (a) to (d) or the polypeptide specified in (e).

5 2. DNA array technology

In one embodiment, the present Invention also provides a method wherein polynucleotide probes are immobilized on a DNA chip in an organised array. Oligonucleotides can be bound to a solid Support by a variety of processes, including
10 lithography. For example a chip can hold up to 4100,00 oligonucleotides (GeneChip, Affymetrix). These polynucleotide probes comprise a nucleotide sequence at least about 12 nucleotides in length, preferably at least about 15 nucleotides, more preferably at least about 25 nucleotides, and most preferably at least about 40 nucleotides, and up to all or nearly all of a sequence which is complementary to a
15 portion of the coding sequence of a marker polynucleotide sequence selected from the polynucleotides of the SEQ ID NOS:1 to 74 and is differentially expressed in cardiovascular tissue. The present invention provides significant advantages over the available tests for cardiovascular disease, such as arteriosclerosis, because it increases the reliability of the test by providing an array of polynucleotide markers on
20 a single chip.

The method includes obtaining a biopsy of an affected artery, which is optionally fractionated by cryostat sectioning to enrich diseased cells to about 80% of the total cell population and the use of body fluids such as serum or urine. The DNA or RNA
25 is then extracted, amplified, and analysed with a DNA chip to determine the presence of absence of the marker polynucleotide sequences. In one embodiment, the polynucleotide probes are spotted onto a substrate in a two-dimensional matrix or array. samples of polynucleotides can be labeled and then hybridised to the probes. Double-stranded polynucleotides, comprising the labeled sample polynucleotides
30 bound to probe polynucleotides, can be detected once the unbound portion of the sample is washed away.

The probe polynucleotides can be spotted on substrates including glass, nitrocellulose, etc. The probes can be bound to the Substrate by either covalent bonds or by non-specific interactions, such as hydrophobic interactions. The sample polynucleotides can be labelled using radioactive labels, fluorophores, chromophores, etc. Techniques for constructing arrays and methods of using these arrays are described in EP No. 0 799 897; PCT No. WO 97/29212; PCT No. WO 97/27317; EP No. 0 785 280; PCT No. WO 97/02357; U.S. Pat. No. 5,593,839; U.S. Pat. No. 5,578,832; EP No. 0 728 520; U.S. Pat. No. 5,599,695; EP No. 0 721 016; U.S. Pat. No. 5,556,752; PCT No. WO 95/22058; and U.S. Pat. No. 5,631,734. Further, arrays can be used to examine differential expression of genes and can be used to determine gene function. For example, arrays of the instant polynucleotide sequences can be used to determine if any of the polynucleotide sequences are differentially expressed between normal cells and diseased cells, for example. High expression of a particular message in a diseased sample, which is not observed in a corresponding normal sample, can indicate a cardiovascular disease specific protein.

Accordingly, in one aspect, the invention provides probes and primers that are specific to the unique polynucleotide markers disclosed herein.

20

In one embodiment, the method comprises using a polynucleotide probe to determine the presence of cardiovascular disease cells in a tissue from a patient. Specifically, the method comprises:

- 1) providing a polynucleotide probe comprising a nucleotide sequence at least 12 nucleotides in length, preferably at least 15 nucleotides, more preferably, 25 nucleotides, and most preferably at least 40 nucleotides, and up to all or nearly all of the coding sequence which is complementary to a portion of the coding sequence of a polynucleotide selected from the polynucleotides or the SEQ ID NOS:1 to 74 or a sequence complementary thereto and is
- 2) differentially expressed in cardiovascular disease, such as arteriosclerosis ;

- 43 -

- 3) obtaining a tissue sample from a patient with cardiovascular disease and arteriosclerosis in particular;
- 4) providing a second tissue sample from a patient with no cardiovascular disease;
- 5) contacting the polynucleotide probe under stringent conditions with RNA of each of said first and second tissue samples (e.g., in a Northern blot or in situ hybridization assay); and
- 6) comparing (a) the amount of hybridization of the probe with RNA of the first tissue sample, with (b) the amount of hybridization of the probe with RNA of the second tissue sample;

wherein a statistically significant difference in the amount of hybridization with the RNA of the first tissue sample as compared to the amount of hybridization with the RNA of the second tissue sample is indicative of cardiovascular disease and arteriosclerosis in particular in the first tissue sample.

3. Detection of variant polynucleotide sequence

In yet another embodiment, the invention provides methods for determining whether a subject is at risk for developing a disease, such as a predisposition to develop cardiovascular disease, for example arteriosclerosis, associated with an aberrant activity of any one of the polypeptides encoded by any of the polynucleotides of the SEQ ID NOS:1 to 74, wherein the aberrant activity of the polypeptide is characterised by detecting the presence or absence of a genetic lesion characterised by at least one of these:

- (i) an alteration affecting the integrity of a gene encoding a marker polypeptides, or
- (ii) the misexpression of the encoding polynucleotide.

To illustrate, such genetic lesions can be detected by ascertaining the existence of at least one of these:

- I. a deletion of one or more nucleotides from the polynucleotide sequence
- 5 II. an addition of one or more nucleotides to the polynucleotide sequence
- III. a Substitution of one or more nucleotides of the polynucleotide sequence
- IV. a gross chromosomal rearrangement of the polynucleotide sequence
- V. a gross alteration in the level of a messenger RNA transcript of the polynucleotide sequence
- 10 VI. aberrant modification of the polynucleotide sequence, such as of the methylation Pattern of the genomic DNA
- VII. the presence of a non-wild type splicing Pattern of a messenger RNA transcript of the gene
- VIII. a non-wild type level of the marker polypeptide
- 15 IX. allelic loss of the gene
- X. inappropriate post-translational modification of the marker polypeptide

The present Invention provides assay techniques for detecting mutations in the encoding polynucleotide sequence. These methods include, but are not limited to, methods involving sequence analysis, Southern blot hybridization, restriction enzyme site mapping, and methods involving detection of absence of nucleotide pairing between the polynucleotide to be analyzed and a probe.

Specific diseases or disorders, e.g., genetic diseases or disorders, are associated with specific allelic variants of polymorphic regions of certain genes, which do not necessarily encode a mutated Protein. Thus, the presence of a specific allelic variant of a polymorphic region of a gene in a subject can render the subject susceptible to developing a specific disease or disorder. Polymorphic regions in genes, can be identified, by determining the nucleotide sequence of genes in populations of individuals. If a polymorphic region is identified, then the link with a specific disease can be determined by studying specific populations of individuals, e.g. individuals

which developed a specific disease, such as cardiovascular disease. A polymorphic region can be located in any region of a gene, e.g., exons, in coding or non coding regions of exons, introns, and promoter region.

5 In an exemplary embodiment, there is provided a polynucleotide composition comprising a polynucleotide probe including a region of nucleotide sequence which is capable of hybridising to a sense or antisense sequence of a gene or naturally occurring mutants thereof, or 5' or 3' flanking sequences or intronic sequences naturally associated with the subject genes or naturally occurring mutants thereof.

10 The polynucleotide of a cell is rendered accessible for hybridization, the probe is contacted with the polynucleotide of the sample, and the hybridization of the probe to the sample polynucleotide is detected. Such techniques can be used to detect lesions or allelic variants at either the genomic or mRNA level, including deletions, substitutions, etc., as well as to determine mRNA transcript levels.

15 A preferred detection method is allele specific hybridization using probes overlapping the mutation or polymorphic site and having about 5, 10, 20, 25, or 30 nucleotides around the mutation or polymorphic region. In a preferred embodiment of the invention, several probes capable of hybridising specifically to allelic variants

20 are attached to a solid phase support, e.g., a "chip". Mutation detection analysis using these chips comprising oligonucleotides, also termed "DNA probe arrays" is described e.g., in Cronin et al. (43). In one embodiment, a chip comprises all the allelic variants of at least one polymorphic region of a gene. The solid phase support is then contacted with a test polynucleotide and hybridization to the specific probes is

25 detected. Accordingly, the identity of numerous allelic variants of one or more genes can be identified in a simple hybridization experiment.

In certain embodiments, detection of the lesion comprises utilizing the probe/primer in a polymerase chain reaction (PCR) (see, e.g. U.S. Patent Nos. 4,683,195 and

30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligase chain reaction (LCR) (see, e.g., Landegran et al., (44) and Nakazawa et al., (45)], the latter

of which can be particularly useful for detecting point mutations in the gene (see Abravaya et al., (46)). In a merely illustrative embodiment, the method includes the steps of (i) collecting a sample of cells from a patient, (ii) isolating polynucleotide (e.g., genomic, mRNA or both) from the cells of the sample, (iii) contacting the
5 polynucleotide sample with one or more primers which specifically hybridise to a polynucleotide sequence under conditions such that hybridization and amplification of the polynucleotide (if present) occurs, and (iv) detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may
10 be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication [Guatelli, J.C. et al., (47)], transcriptional amplification system [Kwoh, D.Y. et al.,
15 (48)], Q-Beta replicase [Lizardi, P.M. et al., (49)], or any other polynucleotide amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of polynucleotide molecules if such molecules are present in very low numbers.

20 In a preferred embodiment of the subject assay, mutations in, or allelic variants, of a gene from a sample cell are identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are
25 determined by gel electrophoresis. Moreover; the use of sequence specific ribozymes (see, for example, U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

4. In situ hybridization

In one aspect, the method comprises *in situ* hybridization with a probe derived from a given marker polynucleotide, which sequence is selected from any of the polynucleotide sequences of the SEQ ID NOS:1 to 74 or a sequence complementary thereto. The method comprises contacting the labeled hybridization probe with a sample of a given type of tissue from a patient potentially having cardiovascular disease and arteriosclerosis in particular as well as normal tissue from a person with no cardiovascular disease, and determining whether the probe labels tissue of the patient to a degree significantly different (e.g., by at least a factor of two, or at least a factor of five, or at least a factor of twenty, or at least a factor of fifty) than the degree to which normal tissue is labelled.

5. Immunohistochemistry

Where tissue samples are employed, immunohistochemical staining may be used to determine the number of cells having the marker polypeptide phenotype. For such staining, a multiblock of tissue is taken from the biopsy or other tissue sample and subjected to proteolytic hydrolysis, employing such agents as protease K or pepsin. In certain embodiments, it may be desirable to isolate a nuclear fraction from the sample cells and detect the level of the marker polypeptide in the nuclear fraction.

The tissues samples are fixed by treatment with a reagent such as formalin, glutaraldehyde, methanol, or the like. The samples are then incubated with an antibody, preferably a monoclonal antibody, with binding specificity for the marker polypeptides. This antibody may be conjugated to a Label for subsequent detection of binding. samples are incubated for a time Sufficient for formation of the immuno-complexes. Binding of the antibody is then detected by virtue of a Label conjugated to this antibody. Where the antibody is unlabelled, a second labelled antibody may be employed, e.g., which is specific for the isotype of the anti-marker polypeptide anti-

- 48 -

body. Examples of Labels which may be employed include radionuclides, fluorescens, chemiluminescens, enzymes and such.

5 Where enzymes are employed, the Substrate for the enzyme may be added to the samples to provide a coloured or fluorescent product. Examples of suitable enzymes for use in conjugates include horseradish peroxidase, alkaline phosphatase, malate dehydrogenase and the like. Where not commercially available, such anti-body-enzyme conjugates are readily produced by techniques known to those skilled in the art.

10

In one embodiment, the assay is performed as a dot blot assay. The dot blot assay finds particular application where tissue samples are employed as it allows determination of the average amount of the marker polypeptide associated with a Single cell by correlating the amount of marker polypeptide in a cell-free extract
15 produced from a predetermined number of cells.

In yet another embodiment, the Invention contemplates using a panel of antibodies which are generated against the marker polypeptides of this invention, which polypeptides are encoded by any of the polynucleotide sequences of the SEQ ID
20 NOS:1 to 74. Such a panel of antibodies may be used as a reliable diagnostic probe for cardiovascular disease. The assay of the present invention comprises contacting a biopsy sample containing cells, e.g., macrophages, with a panel of antibodies to one or more of the encoded products to determine the presence or absence of the marker polypeptides.

25

The diagnostic methods of the subject invention may also be employed as follow-up to treatment, e.g., quantification of the level of marker polypeptides may be indicative of the effectiveness of current or previously employed therapies for cardiovascular diseases and arteriosclerosis in particular as well as the effect of these
30 therapies upon patient prognosis.

The diagnostic assays described above can be adapted to be used as prognostic assays, as well. Such an application takes advantage of the sensitivity of the assays of the Invention to events which take place at characteristic stages in the progression of plaque generation in case of arteriosclerosis. For example, a given marker gene may be up- or down-regulated at a very early stage, perhaps before the cell is developing into a foam cell, while another marker gene may be characteristically up or down regulated only at a much later stage. Such a method could involve the steps of contacting the mRNA of a test cell with a polynucleotide probe derived from a given marker polynucleotide which is expressed at different characteristic levels in cardiovascular disease tissue cells at different stages of arteriosclerosis progression, and determining the approximate amount of hybridization of the probe to the mRNA of the cell, such amount being an indication of the level of expression of the gene in the cell, and thus an indication of the stage of disease progression of the cell; alternatively, the assay can be carried out with an antibody specific for the gene product of the given marker polynucleotide, contacted with the proteins of the test cell. A battery of such tests will disclose not only the existence of a certain arteriosclerotic plaque, but also will allow the clinician to select the mode of treatment most appropriate for the disease, and to predict the likelihood of success of that treatment.

The methods of the invention can also be used to follow the clinical course of a given cardiovascular disease predisposition. For example, the assay of the Invention can be applied to a blood sample from a patient; following treatment of the patient for CVD, another blood sample is taken and the test repeated. Successful treatment will result in removal of demonstrate differential expression, characteristic of the cardiovascular disease tissue cells, perhaps approaching or even surpassing normal levels.

6. Data analysis methods

Comparison of the expression levels of one or more "CVD genes" with reference expression levels, e.g., expression levels in diseased cells of cardiovascular disease or

in normal counterpart cells, is preferably conducted using computer systems. In one embodiment, expression levels are obtained in two cells and these two sets of expression levels are introduced into a computer system for comparison. In a preferred embodiment, one set of expression levels is entered into a computer system for comparison with values that are already present in the computer system, or in computer-readable form that is then entered into the computer system.

In one embodiment, the invention provides a computer readable form of the gene expression profile data of the invention, or of values corresponding to the level of expression of at least one "CVD gene" in a diseased cell. The values can be mRNA expression levels obtained from experiments, e.g., microarray analysis. The values can also be mRNA levels normalised relative to a reference gene whose expression is constant in numerous cells under numerous conditions, e.g., GAPDH. In other embodiments, the values in the computer are ratios of, or differences between, normalised or non-normalized mRNA levels in different samples.

The gene expression profile data can be in the form of a table, such as an Excel table. The data can be alone, or it can be part of a larger database, e.g., comprising other expression profiles. For example, the expression profile data of the invention can be part of a public database. The computer readable form can be in a computer. In another embodiment, the invention provides a computer displaying the gene expression profile data.

In one embodiment, the invention provides a method for determining the similarity between the level of expression of one or more "CVD genes" in a first cell, e.g., a cell of a subject, and that in a second cell, comprising obtaining the level of expression of one or more "CVD genes" in a first cell and entering these values into a computer comprising a database including records comprising values corresponding to levels of expression of one or more "CVD genes" in a second cell, and processor instructions, e.g., a user interface, capable of receiving a selection of one or more values for comparison purposes with data that is stored in the computer. The

computer may further comprise a means for converting the comparison data into a diagram or chart or other type of output.

5 In another embodiment, values representing expression levels of "CVD genes" are entered into a computer system, comprising one or more databases with reference expression levels obtained from more than one cell. For example, the computer comprises expression data of diseased and normal cells. Instructions are provided to the computer, and the computer is capable of comparing the data entered with the data in the computer to determine whether the data entered is more similar to that of
10 a normal cell or of a diseased cell.

In another embodiment, the computer comprises values of expression levels in cells of subjects at different stages of cardiovascular disease, and the computer is capable of comparing expression data entered into the computer with the data stored, and
15 produce results indicating to which of the expression profiles in the computer, the one entered is most similar, such as to determine the stage of cardiovascular disease in the subject.

In yet another embodiment, the reference expression profiles in the computer are
20 expression profiles from cells of cardiovascular disease of one or more subjects, which cells are treated *in vivo* or *in vitro* with a drug used for therapy of cardiovascular disease. Upon entering of expression data of a cell of a subject treated *in vitro* or *in vivo* with the drug, the computer is instructed to compare the data entered to the data in the computer, and to provide results indicating whether the
25 expression data input into the computer are more similar to those of a cell of a subject that is responsive to the drug or more similar to those of a cell of a subject that is not responsive to the drug. Thus, the results indicate whether the subject is likely to respond to the treatment with the drug or unlikely to respond to it.

30 In one embodiment, the invention provides a system that comprises a means for receiving gene expression data for one or a plurality of genes; a means for comparing

the gene expression data from each of said one or plurality of genes to a common reference frame; and a means for presenting the results of the comparison. This system may further comprise a means for clustering the data.

5 In another embodiment, the invention provides a computer program for analysing gene expression data comprising (i) a computer code that receives as input gene expression data for a plurality of genes and (ii) a computer code that compares said gene expression data from each of said plurality of genes to a common reference frame.

10

The invention also provides a machine-readable or computer-readable medium including program instructions for performing the following steps: (i) comparing a plurality of values corresponding to expression levels of one or more genes characteristic of cardiovascular disease in a query cell with a database including records comprising reference expression or expression profile data of one or more reference cells and an annotation of the type of cell; and (ii) indicating to which cell the query cell is most similar based on similarities of expression profiles. The reference cells can be cells from subjects at different stages of cardiovascular disease. The reference cells can also be cells from subjects responding or not responding to a particular drug treatment and optionally incubated *in vitro* or *in vivo* with the drug.

20

The reference cells may also be cells from subjects responding or not responding to several different treatments, and the computer system indicates a preferred treatment for the subject. Accordingly, the invention provides a method for selecting a therapy for a patient having cardiovascular disease, the method comprising: (i) providing the level of expression of one or more genes characteristic of cardiovascular disease in a diseased cell of the patient; (ii) providing a plurality of reference profiles, each associated with a therapy, wherein the subject expression profile and each reference profile has a plurality of values, each value representing the level of expression of a gene characteristic of cardiovascular disease; and (iii) selecting the reference profile most similar to the subject expression profile, to thereby select a therapy for said

25

30

patient. In a preferred embodiment step (iii) is performed by a computer. The most similar reference profile may be selected by weighing a comparison value of the plurality using a weight value associated with the corresponding expression data.

5 The relative abundance of an mRNA in two biological samples can be scored as a perturbation and its magnitude determined (i.e., the abundance is different in the two sources of mRNA tested), or as not perturbed (i.e., the relative abundance is the same). In various embodiments, a difference between the two sources of RNA of at least a factor of about 25% (RNA from one source is 25% more abundant in one
10 source than the other source), more usually about 50%, even more often by a factor of about 2 (twice as abundant), 3 (three times as abundant) or 5 (five times as abundant) is scored as a perturbation. Perturbations can be used by a computer for calculating and expression comparisons.

15 Preferably, in addition to identifying a perturbation as positive or negative, it is advantageous to determine the magnitude of the perturbation. This can be carried out, as noted above, by calculating the ratio of the emission of the two fluorophores used for differential labeling, or by analogous methods that will be readily apparent to those of skill in the art.

20

The computer readable medium may further comprise a pointer to a descriptor of a stage of cardiovascular disease or to a treatment for cardiovascular disease.

In operation, the means for receiving gene expression data, the means for comparing
25 the gene expression data, the means for presenting, the means for normalising, and the means for clustering within the context of the systems of the present invention can involve a programmed computer with the respective functionalities described herein, implemented in hardware or hardware and software; a logic circuit or other component of a programmed computer that performs the operations specifically
30 identified herein, dictated by a computer program; or a computer memory encoded

with executable instructions representing a computer program that can cause a computer to function in the particular fashion described herein.

Those skilled in the art will understand that the systems and methods of the present invention may be applied to a variety of systems, including IBM-compatible personal computers running MS-DOS or Microsoft Windows.

The computer may have internal components linked to external components. The internal components may include a processor element interconnected with a main memory. The computer system can be an Intel Pentium®-based processor of 200 MHz or greater clock rate and with 32 MB or more of main memory. The external component may comprise a mass storage, which can be one or more hard disks (which are typically packaged together with the processor and memory). Such hard disks are typically of 1 GB or greater storage capacity. Other external components include a user interface device, which can be a monitor, together with an inputting device, which can be a "mouse", or other graphic input devices, and/or a keyboard. A printing device can also be attached to the computer.

Typically, the computer system is also linked to a network link, which can be part of an Ethernet link to other local computer systems, remote computer systems, or wide area communication networks, such as the Internet. This network link allows the computer system to share data and processing tasks with other computer systems.

Loaded into memory during operation of this system are several software components, which are both standard in the art and special to the instant invention. These software components collectively cause the computer system to function according to the methods of this invention. These software components are typically stored on a mass storage. A software component represents the operating system, which is responsible for managing the computer system and its network interconnections. This operating system can be, for example, of the Microsoft Windows' family, such as Windows 95, Windows 98, or Windows NT. A software

component represents common languages and functions conveniently present on this system to assist programs implementing the methods specific to this invention. Many high or low level computer languages can be used to program the analytic methods of this invention. Instructions can be interpreted during run-time or
5 compiled. Preferred languages include C/C++, and JAVA[®]. Most preferably, the methods of this invention are programmed in mathematical software packages which allow symbolic entry of equations and high-level specification of processing, including algorithms to be used, thereby freeing a user of the need to procedurally program individual equations or algorithms. Such packages include Matlab from
10 Mathworks (Natick, Mass.), Mathematica from Wolfram Research (Champaign, Ill.), or S-Plus from Math Soft (Cambridge, Mass.). Accordingly, a software component represents the analytic methods of this invention as programmed in a procedural language or symbolic package. In a preferred embodiment, the computer system also contains a database comprising values representing levels of expression of one or
15 more genes characteristic of cardiovascular disease. The database may contain one or more expression profiles of genes characteristic of cardiovascular disease in different cells.

In an exemplary implementation, to practice the methods of the present invention, a
20 user first loads expression profile data into the computer system. These data can be directly entered by the user from a monitor and keyboard, or from other computer systems linked by a network connection, or on removable storage media such as a CD-ROM or floppy disk or through the network. Next the user causes execution of expression profile analysis software which performs the steps of comparing and, e.g.,
25 clustering co-varying genes into groups of genes.

In another exemplary implementation, expression profiles are compared using a method described in U.S. Patent No. 6,203,987. A user first loads expression profile data into the computer system. Geneset profile definitions are loaded into the
30 memory from the storage media or from a remote computer, preferably from a dynamic geneset database system, through the network. Next the user causes

execution of projection software which performs the steps of converting expression profile to projected expression profiles. The projected expression profiles are then displayed.

- 5 In yet another exemplary implementation, a user first leads a projected profile into the memory. The user then causes the loading of a reference profile into the memory. Next, the user causes the execution of comparison software which performs the steps of objectively comparing the profiles.

10 Antisense oligonucleotides

Antisense oligonucleotides are nucleotide sequences which are complementary to a specific DNA or RNA sequence. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form complexes
15 and block either transcription or translation. Preferably, an antisense oligonucleotide is at least 6 nucleotides in length, but can be at least 7, 8, 10, 12, 15, 20, 25, 30, 35, 40, 45, or 50 or more nucleotides long. Longer sequences also can be used. Antisense oligonucleotide molecules can be provided in a DNA construct and introduced into a cell as described above to decrease the level of „CVD gene“ gene products in the
20 cell.

Antisense oligonucleotides can be deoxyribonucleotides, ribonucleotides, peptide nucleic acids (PNAs; described in U.S. Pat. No. 5,714,331), locked nucleic acids (LNAs; described in WO 99/12826), or a combination of them. Oligonucleotides can
25 be synthesised manually or by an automated synthesiser, by covalently linking the 5' end of one nucleotide with the 3' end of another nucleotide with non-phosphodiester internucleotide linkages such as alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, alkylphosphonates, phosphoramidates, phosphate esters, carbamates, acetamidate, carboxymethyl esters, carbonates, and phosphate
30 triesters. See Brown, (50); Sonveaux, (51) and Uhlmann et al., (52).

Modifications of „CVD gene“ expression can be obtained by designing antisense oligonucleotides which will form duplexes to the control, 5', or regulatory regions of the „CVD gene“. Oligonucleotides derived from the transcription initiation site, e.g., between positions 10 and +10 from the start site, are preferred. Similarly, inhibition can be achieved using "triple helix" base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or chaperons. Therapeutic advances using triplex DNA have been described in the literature [e.g., Gee et al., (53)]. An antisense oligonucleotide also can be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Precise complementarity is not required for successful complex formation between an antisense oligonucleotide and the complementary sequence of a „CVD gene“ polynucleotide. Antisense oligonucleotides which comprise, for example, 2, 3, 4, or 5 or more stretches of contiguous nucleotides which are precisely complementary to a „CVD gene“ polynucleotide, each separated by a stretch of contiguous nucleotides which are not complementary to adjacent „CVD gene“ nucleotides, can provide sufficient targeting specificity for „CVD gene“ mRNA. Preferably, each stretch of complementary contiguous nucleotides is at least 4, 5, 6, 7, or 8 or more nucleotides in length. Non-complementary intervening sequences are preferably 1, 2, 3, or 4 nucleotides in length. One skilled in the art can easily use the calculated melting point of an antisense-sense pair to determine the degree of mismatching which will be tolerated between a particular antisense oligonucleotide and a particular „CVD gene“ polynucleotide sequence.

Antisense oligonucleotides can be modified without affecting their ability to hybridise to a „CVD gene“ polynucleotide. These modifications can be internal or at one or both ends of the antisense molecule. For example, internucleoside phosphate linkages can be modified by adding cholesteryl or diamine moieties with varying numbers of carbon residues between the amino groups and terminal ribose. Modified bases and/or sugars, such as arabinose instead of ribose, or a 3', 5' substituted

oligonucleotide in which the 3' hydroxyl group or the 5' phosphate group are substituted, also can be employed in a modified antisense oligonucleotide. These modified oligonucleotides can be prepared by methods well known in the art. See, e.g., Agrawal et al., (54); Uhlmann et al., (52) and Uhlmann et al., (55).

5

Ribozymes

Ribozymes are RNA molecules with catalytic activity. See, e.g., Cech, (56); 1987; Cech, (57) and Couture & Stinchcomb, (58). Ribozymes can be used to inhibit gene
10 function by cleaving an RNA sequence, as is known in the art (e.g., Haseloff et al., U.S. Patent 5,641,673). The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. Examples include engineered hammerhead motif ribozyme molecules that can specifically and efficiently catalyze endonucleo-
15 lytic cleavage of specific nucleotide sequences.

The transcribed sequence of a „CVD gene“ can be used to generate ribozymes which will specifically bind to mRNA transcribed from a „CVD gene“ genomic locus. Methods of designing and constructing ribozymes which can cleave other RNA
20 molecules in trans in a highly sequence specific manner have been developed and described in the art [see Haseloff et al., (59)]. For example, the cleavage activity of ribozymes can be targeted to specific RNAs by engineering a discrete "hybridization" region into the ribozyme. The hybridization region contains a sequence complementary to the target RNA and thus specifically hybridises with the target
25 (see, for example, Gerlach et al., EP No. 0 321201).

Specific ribozyme cleavage sites within a „CVD gene“ RNA target can be identified by scanning the target molecule for ribozyme cleavage sites which include the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences
30 of between 15 and 20 ribonucleotides corresponding to the region of the target RNA containing the cleavage site can be evaluated for secondary structural features which

may render the target inoperable. Suitability of candidate „CVD gene“ RNA targets also can be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays. Longer complementary sequences can be used to increase the affinity of the hybridization sequence for the target. The hybridising and cleavage regions of the ribozyme can be integrally related such that upon hybridising to the target RNA through the complementary regions, the catalytic region of the ribozyme can cleave the target.

Ribozymes can be introduced into cells as part of a DNA construct. Mechanical methods, such as microinjection, liposome-mediated transfection, electroporation, or calcium phosphate precipitation, can be used to introduce a ribozyme-containing DNA construct into cells in which it is desired to decrease „CVD gene“ expression. Alternatively, if it is desired that the cells stably retain the DNA construct, the construct can be supplied on a plasmid and maintained as a separate element or integrated into the genome of the cells, as is known in the art. A ribozyme-encoding DNA construct can include transcriptional regulatory elements, such as a promoter element, an enhancer or UAS element, and a transcriptional terminator signal, for controlling transcription of ribozymes in the cells.

As taught in Haseloff et al., U.S. Pat. No. 5,641,673, ribozymes can be engineered so that ribozyme expression will occur in response to factors which induce expression of a target gene. Ribozymes also can be engineered to provide an additional level of regulation, so that destruction of mRNA occurs only when both a ribozyme and a target gene are induced in the cells.

Polypeptide detection

The subject invention further provides a method of determining whether a cell sample obtained from a subject possesses an abnormal amount of marker polypeptide which comprises (a) obtaining a cell sample from the subject, (b) quantitatively determining the amount of the marker polypeptide in the sample so obtained, and (c)

comparing the amount of the marker polypeptide so determined with a known standard, so as to thereby determine whether the cell sample obtained from the subject possesses an abnormal amount of the marker polypeptide. Such marker polypeptides may be detected by immunohistochemical assays, dot-blot assays, ELISA and the like.

Antibodies

Any type of antibody known in the art can be generated to bind specifically to an epitope of a „CVD gene“ polypeptide. An antibody as used herein includes intact immunoglobulin molecules, as well as fragments thereof, such as Fab, F(ab)₂, and Fv, which are capable of binding an epitope of a „CVD gene“ polypeptide. Typically, at least 6, 8, 10, or 12 contiguous amino acids are required to form an epitope. However, epitopes which involve non-contiguous amino acids may require more, e.g., at least 15, 25, or 50 amino acids.

An antibody which specifically binds to an epitope of a „CVD gene“ polypeptide can be used therapeutically, as well as in immunochemical assays, such as Western blots, ELISAs, radioimmunoassays, immunohistochemical assays, immunoprecipitations, or other immunochemical assays known in the art. Various immunoassays can be used to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays are well known in the art. Such immunoassays typically involve the measurement of complex formation between an immunogen and an antibody which specifically binds to the immunogen.

Typically, an antibody which specifically binds to a „CVD gene“ polypeptide provides a detection signal at least 5-, 10-, or 20-fold higher than a detection signal provided with other proteins when used in an immunochemical assay. Preferably, antibodies which specifically bind to „CVD gene“ polypeptides do not detect other proteins in immunochemical assays and can immunoprecipitate a „CVD gene“ polypeptide from solution.

„CVD gene“ polypeptides can be used to immunize a mammal, such as a mouse, rat, rabbit, guinea pig, monkey, or human, to produce polyclonal antibodies. If desired, a „CVD gene“ polypeptide can be conjugated to a carrier protein, such as bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin. Depending on the host species, various adjuvants can be used to increase the immunological response. Such adjuvants include, but are not limited to, Freund's adjuvant, mineral gels (e.g., aluminum hydroxide), and surface active substances (e.g. lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, and dinitrophenol). Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and *Corynebacterium parvum* are especially useful.

Monoclonal antibodies which specifically bind to a „CVD gene“ polypeptide can be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These techniques include, but are not limited to, the hybridoma technique, the human B cell hybridoma technique, and the EBV hybridoma technique [Kohler et al., (60); Kozbor et al., (61); Cote et al., (62) and Cole et al., (63)].

In addition, techniques developed for the production of chimeric antibodies, the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used [Morrison et al., (64); Neuberger et al., (65); Takeda et al., (66)]. Monoclonal and other antibodies also can be humanized to prevent a patient from mounting an immune response against the antibody when it is used therapeutically. Such antibodies may be sufficiently similar in sequence to human antibodies to be used directly in therapy or may require alteration of a few key residues. Sequence differences between rodent antibodies and human sequences can be minimized by replacing residues which differ from those in the human sequences by site directed mutagenesis of individual residues or by grating of entire complementarity determining regions. Alternatively, humanized antibodies can be produced using recombinant methods, as described in

GB2188638B. Antibodies which specifically bind to a „CVD gene“ polypeptide can contain antigen binding sites which are either partially or fully humanized, as disclosed in U.S. Patent 5,565,332.

5 Alternatively, techniques described for the production of single chain antibodies can be adapted using methods known in the art to produce single chain antibodies which specifically bind to „CVD gene“ polypeptides. Antibodies with related specificity, but of distinct idiotypic composition, can be generated by chain shuffling from random combinatorial immunoglobulin libraries [Burton, (67)].

10

Single-chain antibodies also can be constructed using a DNA amplification method, such as PCR, using hybridoma cDNA as a template [Thirion et al., (68)]. Single-chain antibodies can be mono- or bispecific, and can be bivalent or tetravalent. Construction of tetravalent, bispecific single-chain antibodies is taught, for example,
15 in Coloma & Morrison, (69). Construction of bivalent, bispecific single-chain antibodies is taught in Mallender & Voss, (70).

20

A nucleotide sequence encoding a single-chain antibody can be constructed using manual or automated nucleotide synthesis, cloned into an expression construct using standard recombinant DNA methods, and introduced into a cell to express the coding sequence, as described below. Alternatively, single-chain antibodies can be produced directly using, for example, filamentous phage technology [Verhaar et al., (71); Nicholls et al., (72)].

25

Antibodies which specifically bind to „CVD gene“ polypeptides also can be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature [Orlandi et al., (73) and Winter et al., (74)].

30

Other types of antibodies can be constructed and used therapeutically in methods of the invention. For example, chimeric antibodies can be constructed as disclosed in

WO 93/03151. Binding proteins which are derived from immunoglobulins and which are multivalent and multispecific, such as the antibodies described in WO 94/13804, also can be prepared.

5 Antibodies according to the invention can be purified by methods well known in the art. For example, antibodies can be affinity purified by passage over a column to which a „CVD gene“ polypeptide is bound. The bound antibodies can then be eluted from the column using a buffer with a high salt concentration.

10 Immunoassays are commonly used to quantify the levels of proteins in cell samples, and many other immunoassay techniques are known in the art. The invention is not limited to a particular assay procedure, and therefore is intended to include both homogeneous and heterogeneous procedures. Exemplary immunoassays which can be conducted according to the invention include fluorescence polarisation
15 immunoassay (FPIA), fluorescence immunoassay (FIA), enzyme immunoassay (ELA), nephelometric inhibition immunoassay (NIA), enzyme linked immunosorbent assay (ELISA), and radioimmunoassay (RIA). An indicator moiety, or label group, can be attached to the subject antibodies and is selected so as to meet the needs of various uses of the method which are often dictated by the availability of assay
20 equipment and compatible immunoassay procedures. General techniques to be used in performing the various immunoassays noted above are known to those of ordinary skill in the art.

In another embodiment, the level of the encoded product, i.e., the product encoded by
25 any of the polynucleotide sequences of the SEQ ID NOS:1 to 74 or a sequence complementary thereto, in a biological fluid (e.g., blood or urine) of a patient may be determined as a way of monitoring the level of expression of the marker polynucleotide sequence in cells of that patient. Such a method would include the steps of obtaining a sample of a biological fluid from the patient, contacting the
30 sample (or proteins from the sample) with an antibody specific for a encoded marker polypeptide, and determining the amount of immune complex formation by the

antibody, with the amount of immune complex formation being indicative of the level of the marker encoded product in the sample. This determination is particularly instructive when compared to the amount of immune complex formation by the same antibody in a control sample taken from a normal individual or in one or more samples previously or subsequently obtained from the same person.

In another embodiment, the method can be used to determine the amount of marker polypeptide present in a cell, which in turn can be correlated with progression of the disorder, e.g., plaque formation. The level of the marker polypeptide can be used predictively to evaluate whether a sample of cells contains cells which are, or are predisposed towards becoming, plaque associated cells. The observation of marker polypeptide level can be utilized in decisions regarding, e.g., the use of more stringent therapies.

As set out above, one aspect of the present invention relates to diagnostic assays for determining, in the context of cells isolated from a patient, if the level of a marker polypeptide is significantly reduced in the sample cells. The term "significantly reduced" refers to a cell phenotype wherein the cell possesses a reduced cellular amount of the marker polypeptide relative to a normal cell of similar tissue origin. For example, a cell may have less than about 50%, 25%, 10%, or 5% of the marker polypeptide that a normal control cell. In particular, the assay evaluates the level of marker polypeptide in the test cells, and, preferably, compares the measured level with marker polypeptide detected in at least one control cell, e.g., a normal cell and/or a transformed cell of known phenotype.

Of particular importance to the subject invention is the ability to quantify the level of marker polypeptide as determined by the number of cells associated with a normal or abnormal marker polypeptide level. The number of cells with a particular marker polypeptide phenotype may then be correlated with patient prognosis. In one embodiment of the invention, the marker polypeptide phenotype of the lesion is determined as a percentage of cells in a biopsy which are found to have abnormally

high/low levels of the marker polypeptide. Such expression may be detected by immunohistochemical assays, dot-blot assays, ELISA and the like.

Polypeptide activity

5

In one embodiment the present invention provides a method for screening potentially therapeutic agents which modulate the activity of one or more "CVD gene" polypeptides, such that if the activity of the polypeptide is increased as a result of the upregulation of the "CVD gene" in a subject having or at risk for cardiovascular disease and arteriosclerosis in particular, the therapeutic substance will decrease the activity of the polypeptide relative to the activity of the same polypeptide in a subject not having or not at risk for cardiovascular diseases or arteriosclerosis in particular but not treated with the therapeutic agent. Likewise, if the activity of the polypeptide as a result of the downregulation of the "CVD gene" is decreased in a subject having or at risk for cardiovascular disease or arteriosclerosis in particular, the therapeutic agent will increase the activity of the polypeptide relative to the activity of the same polypeptide in a subject not having or not at risk for cardiovascular disease or arteriosclerosis in particular, but not treated with the therapeutic agent.

20 The activity of the "CVD gene" polypeptides indicated in Table 4 may be measured by any means known to those of skill in the art, and which are particular for the type of activity performed by the particular polypeptide. Examples of specific assays which may be used to measure the activity of particular polynucleotides are shown below.

25

a) G protein coupled receptors

In one embodiment, the "CVD gene" polynucleotide may encode a G protein coupled receptor. In one embodiment, the present invention provides a method of screening potential modulators (inhibitors or activators) of the G protein coupled receptor by

30

measuring changes in the activity of the receptor in the presence of a candidate modulator.

1. G_i -coupled receptors

5

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor and with an inducible CRE-luciferase construct. Cells are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 10% CO₂ and are routinely split at a ratio of 1:10 every 2 or 3 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). Growth medium is then exchanged against serum free medium (SFM; e.g. Ultra-CHO), containing 0,1% BSA. Test compounds dissolved in DMSO are diluted in SFM and transferred to the test cultures (maximal final concentration 10 µmolar), followed by addition of forskolin (~ 1 µmolar, final conc.) in SFM + 0,1% BSA 10 minutes later. In case of antagonist screening both, an appropriate concentration of agonist, and forskolin are added. The plates are incubated at 37°C in 10% CO₂ for 3 hours. Then the supernatant is removed, cells are lysed with lysis reagent (25 mmolar phosphate-buffer, pH 7,8 , containing 2 mmolar DDT, 10% glycerol and 3% Triton X100). The luciferase reaction is started by addition of substrate-buffer (e.g. luciferase assay reagent, Promega) and luminescence is immediately determined (e.g. Berthold luminometer or Hamamatsu camera system).

25

2. G_s -coupled receptors

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor and with an inducible CRE-luciferase construct. Cells are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 10% CO₂ and are routinely split

30

at a ratio of 1:10 every 2 or 3 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 1000 or 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). The assay is started by addition of test-compounds in serum free medium (SFM; e.g. Ultra-CHO) containing 0,1% BSA: Test compounds are dissolved in DMSO, diluted in SFM and transferred to the test cultures (maximal final concentration 10 µmolar, DMSO conc. < 0,6 %). In case of antagonist screening an appropriate concentration of agonist is added 5 – 10 minutes later. The plates are incubated at 37°C in 10% CO₂ for 3 hours. Then the cells are lysed with 10 µl lysis reagent per well (25 mmolar phosphate-buffer, pH 7,8 , containing 2 mmolar DDT, 10% glycerol and 3% Triton X100) and the luciferase reaction is started by addition of 20 µl substrate-buffer per well (e.g. luciferase assay reagent, Promega). Measurement of luminescence is started immediately (e.g. Berthold luminometer or Hamamatzu camera system).

15

3. G_q–coupled receptors

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor. Cells expressing functional receptor protein are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 5% CO₂ and are routinely split at a cell line dependent ratio every 3 or 4 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). Growth medium is then exchanged against physiological salt solution (e.g. Tyrode solution). Test compounds dissolved in DMSO are diluted in Tyrode solution containing 0.1% BSA and transferred to the test cultures (maximal final concentration 10 µmolar). After addition of the receptor specific agonist the

30

resulting Gq-mediated intracellular calcium increase is measured using appropriate read-out systems (e.g. calcium-sensitive dyes).

b) Ion channels

5

Ion channels are integral membrane proteins involved in electrical signaling, transmembrane signal transduction, and electrolyte and solute transport. By forming macromolecular pores through the membrane lipid bilayer, ion channels account for the flow of specific ion species driven by the electrochemical potential gradient for the permeating ion. At the single molecule level, individual channels undergo conformational transitions ("gating") between the 'open' (ion conducting) and 'closed' (non conducting) state. Typical single channel openings last for a few milliseconds and result in elementary transmembrane currents in the range of 10^{-9} - 10^{-12} Ampere. Channel gating is controlled by various chemical and/or biophysical parameters, such as neurotransmitters and intracellular second messengers ('ligand-gated' channels) or membrane potential ('voltage-gated' channels). Ion channels are functionally characterised by their ion selectivity, gating properties, and regulation by hormones and pharmacological agents. Because of their central role in signaling and transport processes, ion channels present ideal targets for pharmacological therapeutics in various pathophysiological settings.

15

20

Screening for compounds interacting with ion channels to either inhibit or promote their activity can be based on (1.) binding and (2.) functional assays in living cells (110).

25

30

In one embodiment, the "CVD gene" may encode an ion channel. In one embodiment, the present invention provides a method of screening potential activators or inhibitors of channels activity of the "CVD gene" polypeptide. Screening for compounds interaction with ion channels to either inhibit or promote their activity can be based on (1.) binding and (2.) functional assays in living cells. See e.g. Hille (110).

1. For ligand-gated channels, e.g. ionotropic neurotransmitter/hormone receptors, assays can be designed detecting binding to the target by competition between the compound and a labeled ligand.
2. Ion channel function can be tested functionally in living cells. Target proteins are either expressed endogenously in appropriate reporter cells or are introduced recombinantly. Channel activity can be monitored by (2.1) concentration changes of the permeating ion (most prominently Ca^{2+} ions), (2.2) by changes in the transmembrane electrical potential gradient, and (2.3) by measuring a cellular response (e.g. expression of a reporter gene, secretion of a neurotransmitter) triggered or modulated by the target activity.
 - 2.1 Channel activity results in transmembrane ion fluxes. Thus activation of ionic channels can be monitored by the resulting changes in intracellular ion concentrations using luminescent or fluorescent indicators. Because of its wide dynamic range and availability of suitable indicators this applies particularly to changes in intracellular Ca^{2+} ion concentration ($[\text{Ca}^{2+}]_i$). $[\text{Ca}^{2+}]_i$ can be measured, for example, by aequorin luminescence or fluorescence dye technology (e.g. using Fluo-3, Indo-1, Fura-2). Cellular assays can be designed where either the Ca^{2+} flux through the target channel itself is measured directly or where modulation of the target channel affects membrane potential and thereby the activity of co-expressed voltage-gated Ca^{2+} channels.
 - 2.2 Ion channel currents result in changes of electrical membrane potential (V_m) which can be monitored directly using potentiometric fluorescent probes. These electrically charged indicators (e.g. the anionic oxonol dye DiBAC₄(3)) redistribute between extra- and intracellular compartment in response to voltage changes. The equilibrium distribution is governed by the Nernst-equation. Thus changes in membrane potential results in concomitant changes in cellular fluorescence. Again, changes in V_m might be caused directly by the activity of the target ion channel or through amplification and/or prolongation of the signal by channels co-expressed in the same cell.

2.3 Target channel activity can cause cellular Ca^{2+} entry either directly or through activation of additional Ca^{2+} channel (see 2.1). The resulting intracellular Ca^{2+} signals regulate a variety of cellular responses, e.g. secretion or gene transcription. Therefore modulation of the target channel can be detected by monitoring secretion of a known hormone/transmitter from the target-expressing cell or through expression of a reporter gene (e.g. luciferase) controlled by an Ca^{2+} -responsive promoter element (e.g. cyclic AMP/ Ca^{2+} -responsive elements; CRE).

10 c) DNA-binding proteins and transcription factors

In one embodiment, the "CVD gene" may encode a DNA-binding protein or a transcription factor. The activity of such a DNA-binding protein or a transcription factor may be measured, for example, by a promoter assay which measures the ability of the DNA-binding protein or the transcription factor to initiate transcription of a test sequence linked to a particular promoter. In one embodiment, the present invention provides a method of screening test compounds for its ability to modulate the activity of such a DNA-binding protein or a transcription factor by measuring the changes in the expression of a test gene which is regulated by a promoter which is responsive to the transcription factor.

Promotor assays

A promoter assay was set up with a human hepatocellular carcinoma cell HepG2 that was stably transfected with a luciferase gene under the control of a gene of interest (e.g. thyroid hormone) regulated promoter. The vector 2xIROluc, which was used for transfection, carries a thyroid hormone responsive element (TRE) of two 12 bp inverted palindromes separated by an 8 bp spacer in front of a tk minimal promoter and the luciferase gene. Test cultures were seeded in 96 well plates in serum - free Eagle's Minimal Essential Medium supplemented with glutamine, tricine, sodium pyruvate, non - essential amino acids, insulin, selen, transferrin, and were cultivated

in a humidified atmosphere at 10 % CO₂ at 37°C. After 48 hours of incubation serial dilutions of test compounds or reference compounds (L-T3, L-T4 e.g.) and costimulator if appropriate (final concentration 1 nM) were added to the cell cultures and incubation was continued for the optimal time (e.g. another 4-72 hours). The cells were then lysed by addition of buffer containing Triton X100 and luciferin and the luminescence of luciferase induced by T3 or other compounds was measured in a luminometer. For each concentration of a test compound replicates of 4 were tested. EC₅₀ – values for each test compound were calculated by use of the Graph Pad Prism Scientific software.

10

Screening Methods

The invention provides assays for screening test compounds which bind to or modulate the activity of a „CVD gene“ polypeptide or a „CVD gene“ polynucleotide. A test compound preferably binds to a „CVD gene“ polypeptide or polynucleotide. More preferably, a test compound decreases or increases „CVD gene“ activity by at least about 10, preferably about 50, more preferably about 75, 90, or 100% relative to the absence of the test compound.

15

1. Test Compounds

20

Test compounds can be pharmacological agents already known in the art or can be compounds previously unknown to have any pharmacological activity. The compounds can be naturally occurring or designed in the laboratory. They can be isolated from microorganisms, animals, or plants, and can be produced recombinant, or synthesised by chemical methods known in the art. If desired, test compounds can be obtained using any of the numerous combinatorial library methods known in the art, including but not limited to, biological libraries, spatially addressable parallel solid phase or solution phase libraries, synthetic library methods requiring deconvolution, the one-bead one-compound library method, and synthetic library methods using affinity chromatography selection. The biological library approach is limited to polypeptide libraries, while the other four approaches are applicable to

25

30

polypeptide, non-peptide oligomer, or small molecule libraries of compounds. [For review see Lam, (75)].

Methods for the synthesis of molecular libraries are well known in the art [see, for example, DeWitt et al., (76); Erb et al., (77); Zuckermann et al., (78); Cho et al., (79); Carell et al., (80) and Gallop et al., (81). Libraries of compounds can be presented in solution [see, e.g., Houghten, (82)], or on beads [Lam, (83)], chips [Fodor, (84)], bacteria or spores (Ladner, U.S. Patent 5,223,409), plasmids [Cull et al., (85)], or phage [Scott & Smith, (86); Devlin, (87); Cwirla et al., (88); Felici, (89)].

High Throughput Screening

Test compounds can be screened for the ability to bind to „CVD gene“ polypeptides or polynucleotides or to affect „CVD gene“ activity or „CVD gene“ expression using high throughput screening. Using high throughput screening, many discrete compounds can be tested in parallel so that large numbers of test compounds can be quickly screened. The most widely established techniques utilize 96-well microtiter plates. The wells of the microtiter plates typically require assay volumes that range from 50 to 500 µl. In addition to the plates, many instruments, materials, pipettors, robotics, plate washers, and plate readers are commercially available to fit the 96-well format.

Alternatively, free format assays, or assays that have no physical barrier between samples, can be used. For example, an assay using pigment cells (melanocytes) in a simple homogeneous assay for combinatorial peptide libraries is described by Jayawickreme et al., (90). The cells are placed under agarose in culture dishes, then beads that carry combinatorial compounds are placed on the surface of the agarose. The combinatorial compounds are partially released the compounds from the beads.

Active compounds can be visualised as dark pigment areas because, as the compounds diffuse locally into the gel matrix, the active compounds cause the cells to change colours.

5 Another example of a free format assay is described by Chelsky, (91), reported at the First Annual Conference of The Society for Biomolecular Screening in Philadelphia, (1995). Chelsky placed a simple homogenous enzyme assay for carbonic anhydrase inside an agarose gel such that the enzyme in the gel would cause a colour change throughout the gel. Thereafter, beads carrying combinatorial compounds via a photo-
10 linker were placed inside the gel and the compounds were partially released by UV light. Compounds that inhibited the enzyme were observed as local zones of inhibition having less colour change.

Yet another example is described by Salmon et al., (92). In this example, combinatorial libraries were screened for compounds that had cytotoxic effects on
15 cancer cells growing in agar.

Another high throughput screening method is described in Beutel et al., U.S. Patent 5,976,813. In this method, test samples are placed in a porous matrix. One or more assay components are then placed within, on top of, or at the bottom of a matrix such
20 as a gel, a plastic sheet, a filter, or other form of easily manipulated solid support. When samples are introduced to the porous matrix they diffuse sufficiently slowly, such that the assays can be performed without the test samples running together.

Binding Assays

25

For binding assays, the test compound is preferably a small molecule which binds to and occupies, for example, the ATP/GTP binding site of the enzyme or the active site of a „CVD gene“ polypeptide, such that normal biological activity is prevented. Examples of such small molecules include, but are not limited to, small peptides or
30 peptide-like molecules.

In binding assays, either the test compound or a „CVD gene“ polypeptide can comprise a detectable label, such as a fluorescent, radioisotopic, chemiluminescent, or enzymatic label, such as horseradish peroxidase, alkaline phosphatase, or luciferase. Detection of a test compound which is bound to a „CVD gene“ polypeptide can then be accomplished, for example, by direct counting of radioemmission, by scintillation counting, or by determining conversion of an appropriate substrate to a detectable product.

Alternatively, binding of a test compound to a „CVD gene“ polypeptide can be determined without labeling either of the interactants. For example, a microphysiometer can be used to detect binding of a test compound with a „CVD gene“ polypeptide. A microphysiometer (e.g., CytosensorJ) is an analytical instrument that measures the rate at which a cell acidifies its environment using a light-addressable potentiometric sensor (LAPS). Changes in this acidification rate can be used as an indicator of the interaction between a test compound and a „CVD gene“ polypeptide [McConnell et al., (93)].

Determining the ability of a test compound to bind to a „CVD gene“ polypeptide also can be accomplished using a technology such as real-time Bimolecular Interaction Analysis (BIA) [Sjolander & Urbaniczky, (94), and Szabo et al., (95)]. BIA is a technology for studying biospecific interactions in real time, without labeling any of the interactants (e.g., BIAcoreTM). Changes in the optical phenomenon surface plasmon resonance (SPR) can be used as an indication of real-time reactions between biological molecules.

In yet another aspect of the invention, a „CVD gene“ polypeptide can be used as a "bait protein" in a two-hybrid assay or three-hybrid assay (see, e.g., U.S. Patent 5,283,317; Zervos et al., (96); Madura et al., (97); Bartel et al., (98); Iwabuchi et al., (99) and Brent WO 94/10300), to identify other proteins which bind to or interact with the „CVD gene“ polypeptide and modulate its activity.

- 75 -

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. For example, in one construct, polynucleotide encoding a „CVD gene“ polypeptide can be fused to a polynucleotide encoding the DNA binding domain of a known transcription factor (e.g., GAL4). In the other construct a DNA sequence that encodes an unidentified protein ("prey" or "sample") can be fused to a polynucleotide that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact in vivo to form an protein- dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ), which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected, and cell colonies containing the functional transcription factor can be isolated and used to obtain the DNA sequence encoding the protein which interacts with the „CVD gene“ polypeptide.

It may be desirable to immobilise either a „CVD gene“ polypeptide (or polynucleotide) or the test compound to facilitate separation of bound from unbound forms of one or both of the interactants, as well as to accommodate automation of the assay. Thus, either a „CVD gene“ polypeptide (or polynucleotide) or the test compound can be bound to a solid support. Suitable solid supports include, but are not limited to, glass or plastic slides, tissue culture plates, microtiter wells, tubes, silicon chips, or particles such as beads (including, but not limited to, latex, polystyrene, or glass beads). Any method known in the art can be used to attach a „CVD gene“ polypeptide (or polynucleotide) or test compound to a solid support, including use of covalent and non-covalent linkages, passive absorption, or pairs of binding moieties attached respectively to the polypeptide (or polynucleotide) or test compound and the solid support. Test compounds are preferably bound to the solid support in an array, so that the location of individual test compounds can be tracked. Binding of a test compound to a „CVD gene“ polypeptide (or polynucleotide) can be

accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and microcentrifuge tubes.

5 In one embodiment, a „CVD gene“ polypeptide is a fusion protein comprising a domain that allows the „CVD gene“ polypeptide to be bound to a solid support. For example, glutathione S-transferase fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, Mo.) or glutathione derivatized microtiter plates, which are then combined with the test compound or the test compound and the nonadsorbed „CVD gene“ polypeptide; the mixture is then
10 incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components. Binding of the interactants can be determined either directly or indirectly, as described above. Alternatively, the complexes can be dissociated from the solid support before binding is determined.

15 Other techniques for immobilising proteins or polynucleotides on a solid support also can be used in the screening assays of the invention. For example, either a „CVD gene“ polypeptide (or polynucleotide) or a test compound can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated „CVD gene“ polypeptides (or polynucleotides) or test compounds can be prepared from biotin
20 NHS (N-hydroxysuccinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, Ill.) and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies which specifically bind to a „CVD gene“ polypeptide, polynucleotide, or a test compound, but which do not interfere with a desired binding site, such as the ATP/GTP binding
25 site or the active site of the „CVD gene“ polypeptide, can be derivatised to the wells of the plate. Unbound target or protein can be trapped in the wells by antibody conjugation.

30 Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies which specifically bind to a „CVD gene“ polypeptide or test compound,

enzyme-linked assays which rely on detecting an activity of a „CVD gene“ polypeptide, and SDS gel electrophoresis under non-reducing conditions.

5 Screening for test compounds which bind to a „CVD gene“ polypeptide or polynucleotide also can be carried out in an intact cell. Any cell which comprises a „CVD gene“ polypeptide or polynucleotide can be used in a cell-based assay system. A „CVD gene“ polynucleotide can be naturally occurring in the cell or can be introduced using techniques such as those described above. Binding of the test compound to a „CVD gene“ polypeptide or polynucleotide is determined as
10 described above.

Modulation of Gene Expression

15 In another embodiment, test compounds which increase or decrease „CVD gene“ expression are identified. A „CVD gene“ polynucleotide is contacted with a test compound, and the expression of an RNA or polypeptide product of the „CVD gene“ polynucleotide is determined. The level of expression of appropriate mRNA or polypeptide in the presence of the test compound is compared to the level of expression of mRNA or polypeptide in the absence of the test compound. The test compound
20 can then be identified as a modulator of expression based on this comparison. For example, when expression of mRNA or polypeptide is greater in the presence of the test compound than in its absence, the test compound is identified as a stimulator or enhancer of the mRNA or polypeptide expression. Alternatively, when expression of the mRNA or polypeptide is less in the presence of the test compound than in its
25 absence, the test compound is identified as an inhibitor of the mRNA or polypeptide expression.

The level of „CVD gene“ mRNA or polypeptide expression in the cells can be determined by methods well known in the art for detecting mRNA or polypeptide.
30 Either qualitative or quantitative methods can be used. The presence of polypeptide products of a „CVD gene“ polynucleotide can be determined, for example, using a

variety of techniques known in the art, including immunochemical methods such as radioimmunoassay, Western blotting, and immunohistochemistry. Alternatively, polypeptide synthesis can be determined in vivo, in a cell culture, or in an in vitro translation system by detecting incorporation of labelled amino acids into a „CVD gene“ polypeptide.

Such screening can be carried out either in a cell-free assay system or in an intact cell. Any cell which expresses a „CVD gene“ polynucleotide can be used in a cell-based assay system. A „CVD gene“ polynucleotide can be naturally occurring in the cell or can be introduced using techniques such as those described above. Either a primary culture or an established cell line, such as CHO or human embryonic kidney 293 cells, can be used.

Therapeutic Indications and Methods

Therapies for treatment of CVD primarily relied upon effective drugs for lowering cholesterol and high blood pressure. In particular, the statins lower levels of arteriogenic lipoproteins and dramatically decrease clinical events and mortality from arteriosclerosis. Nevertheless, heart disease and stroke remain by far the most common causes of death in westernised societies, and new weapons, particularly agents that block disease at the level of the vessel wall or that raise anti-arteriogenic HDL, are needed. The advent of genomics-driven molecular target identification has opened up the possibility of identifying new cardiovascular disease-specific targets for therapeutic intervention that will provide safer, more effective treatments for CVD patients and arteriosclerosis patients in particular. Thus, newly discovered CVD-associated genes and their products can be tested for their role(s) in disease and used as tools to discover and develop innovative therapies. The identification of the ABC transporter presents exciting new opportunities for treatment of low HDL levels. Preliminary studies in animals suggest that it may be possible not only to block the development of arteriosclerosis but also to achieve significant regression. The most critical clinical aspect of arteriosclerosis is plaque rupture and thrombosis.

Genes playing important roles in any of the physiological processes outlined above can be characterized as cardiovascular disease targets. Genes or gene fragments identified through genomics can readily be expressed in one or more heterologous expression systems to produce functional recombinant proteins. These proteins are characterised in vitro for their biochemical properties and then used as tools in high-throughput molecular screening programs to identify chemical modulators of their biochemical activities. Modulators of target protein activity can be identified in this manner and subsequently tested in cellular and in vivo disease models for therapeutic activity. Optimisation of lead compounds with iterative testing in biological models and detailed pharmacokinetic and toxicological analyses form the basis for drug development and subsequent testing in humans.

The activities of the „CVD genes“ provide therapeutic targets for cardiovascular disease and arteriosclerosis in particular.

This invention further pertains to the use of novel agents identified by the screening assays described above. Accordingly, it is within the scope of this invention to use a test compound identified as described herein in an appropriate animal model. For example, an agent identified as described herein (e.g., a modulating agent, an antisense nucleic acid molecule, a specific antibody, ribozyme, or a human „CVD gene“ polypeptide binding molecule) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above described screening assays for treatments as described herein.

A reagent which affects human „CVD gene“ activity can be administered to a human cell, either in vitro or in vivo, to reduce or increase human „CVD gene“ activity. The reagent preferably binds to an expression product of a human „CVD gene“. If the

expression product is a protein, the reagent is preferably an antibody. For treatment of human cells ex vivo, an antibody can be added to a preparation of stem cells which have been removed from the body. The cells can then be replaced in the same or another human body, with or without clonal propagation, as is known in the art.

5

In one embodiment, the reagent is delivered using a liposome. Preferably, the liposome is stable in the animal into which it has been administered for at least about 30 minutes, more preferably for at least about 1 hour, and even more preferably for at least about 24 hours. A liposome comprises a lipid composition that is capable of

10 targeting a reagent, particularly a polynucleotide, to a particular site in an animal, such as a human. Preferably, the lipid composition of the liposome is capable of targeting to a specific organ of an animal, such as the lung, liver, spleen, heart brain, lymph nodes, and skin.

15

A liposome useful in the present invention comprises a lipid composition that is capable of fusing with the plasma membrane of the targeted cell to deliver its contents to the cell. Preferably, the transfection efficiency of a liposome is about 0.5 μg of DNA per 16 nmol of liposome delivered to about 10^6 cells, more preferably about 1.0 μg of DNA per 16 nmol of liposome delivered to about 10^6 cells, and even

20 more preferably about 2.0 μg of DNA per 16 nmol of liposome delivered to about 10^6 cells. Preferably, a liposome is between about 100 and 500 nm, more preferably between about 150 and 450 nm, and even more preferably between about 200 and 400 nm in diameter.

25

Suitable liposomes for use in the present invention include those liposomes usually used in, for example, gene delivery methods known to those of skill in the art. More preferred liposomes include liposomes having a polycationic lipid composition and/or liposomes having a cholesterol backbone conjugated to polyethylene glycol. Optionally, a liposome comprises a compound capable of targeting the liposome to a

30 particular cell type, such as a cell-specific ligand exposed on the outer surface of the liposome.

Complexing a liposome with a reagent such as an antisense oligonucleotide or ribozyme can be achieved using methods which are standard in the art (see, for example, U.S. Patent 5,705,151). Preferably, from about 0.1 μg to about 10 μg of polynucleotide is combined with about 8 nmol of liposomes, more preferably from about 0.5 μg to about 5 μg of polynucleotides are combined with about 8 nmol liposomes, and even more preferably about 1.0 μg of polynucleotides is combined with about 8 nmol liposomes.

In another embodiment, antibodies can be delivered to specific tissues in vivo using receptor-mediated targeted delivery. Receptor-mediated DNA delivery techniques are taught in, for example, Findeis et al., (100); Chiou et al., (101); Wu & Wu, (102); Wu et al., (103); Zenke et al., (104); Wu et al., (105).

Determination of a Therapeutically Effective Dose

The determination of a therapeutically effective dose is well within the capability of those skilled in the art. A therapeutically effective dose refers to that amount of active ingredient which increases or decreases human „CVD gene“ activity relative to the human „CVD gene“ activity which occurs in the absence of the therapeutically effective dose.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays or in animal models, usually mice, rabbits, dogs, or pigs. The animal model also can be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

Therapeutic efficacy and toxicity, e.g., ED_{50} (the dose therapeutically effective in 50% of the population) and LD_{50} (the dose lethal to 50% of the population), can be determined by standard pharmaceutical procedures in cell cultures or experimental

animals. The dose ratio of toxic to therapeutic effects is the therapeutic index, and it can be expressed as the ratio, LD_{50}/ED_{50} .

Pharmaceutical compositions which exhibit large therapeutic indices are preferred.

5 The data obtained from cell culture assays and animal studies is used in formulating a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, sensitivity of the patient, and the route of administration.

10

The exact dosage will be determined by the practitioner, in light of factors related to the subject that requires treatment. Dosage and administration are adjusted to provide sufficient levels of the active ingredient or to maintain the desired effect. Factors which can be taken into account include the severity of the disease state, general
15 health of the subject, age, weight, and gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting pharmaceutical compositions can be administered every 3 to 4 days, every week, or once every two weeks depending on the half-life and clearance rate of the particular formulation.

20

Normal dosage amounts can vary from 0.1 to 100,000 micrograms, up to a total dose of about 1 g, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations
25 for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

30

If the reagent is a single-chain antibody, polynucleotides encoding the antibody can be constructed and introduced into a cell either ex vivo or in vivo using well-established techniques including, but not limited to, transferrin-polycation-mediated

DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, a gene gun, and DEAE- or calcium phosphate-mediated transfection.

5

Effective in vivo dosages of an antibody are in the range of about 5 µg to about 50 µg/kg, about 50 µg to about 5 mg/kg, about 100 µg to about 500 µg/kg of patient body weight, and about 200 to about 250 µg/kg of patient body weight. For administration of polynucleotides encoding single-chain antibodies, effective in vivo
10 dosages are in the range of about 100 ng to about 200 ng, 500 ng to about 50 mg, about 1 µg to about 2 mg, about 5 µg to about 500 µg, and about 20 µg to about 100 µg of DNA.

If the expression product is mRNA, the reagent is preferably an antisense
15 oligonucleotide or a ribozyme. Polynucleotides which express antisense oligonucleotides or ribozymes can be introduced into cells by a variety of methods, as described above.

Preferably, a reagent reduces expression of a „CVD gene“ gene or the activity of a
20 „CVD gene“ polypeptide by at least about 10, preferably about 50, more preferably about 75, 90, or 100% relative to the absence of the reagent. The effectiveness of the mechanism chosen to decrease the level of expression of a „CVD gene“ gene or the activity of a „CVD gene“ polypeptide can be assessed using methods well known in the art, such as hybridization of nucleotide probes to „CVD gene“ -specific mRNA,
25 quantitative RT-PCR, immunologic detection of a „CVD gene“ polypeptide, or measurement of „CVD gene“ activity.

In any of the embodiments described above, any of the pharmaceutical compositions of the invention can be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy can
30 be made by one of ordinary skill in the art, according to conventional pharmaceutical

principles. The combination of therapeutic agents can act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

5

Any of the therapeutic methods described above can be applied to any subject in need of such therapy, including, for example, birds and mammals such as dogs, cats, cows, pigs, sheep, goats, horses, rabbits, monkeys, and most preferably, humans.

10

All patents and patent applications cited in this disclosure are expressly incorporated herein by reference. The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples which are provided for purposes of illustration only and are not intended to limit the scope of the invention.

15

Pharmaceutical Compositions

20

The invention also provides pharmaceutical compositions which can be administered to a patient to achieve a therapeutic effect. Pharmaceutical compositions of the invention can comprise, for example, a „CVD gene“ polypeptide, „CVD gene“ polynucleotide, ribozymes or antisense oligonucleotides, antibodies which specifically bind to a „CVD gene“ polypeptide, or mimetics, agonists, antagonists, or inhibitors of a „CVD gene“ polypeptide activity. The compositions can be administered alone or in combination with at least one other agent, such as stabilizing compound, which

can be administered in any sterile, biocompatible pharmaceutical carrier, including, but not limited to, saline, buffered saline, dextrose, and water. The compositions can be administered to a patient alone, or in combination with other agents, drugs or hormones.

25

30

In addition to the active ingredients, these pharmaceutical compositions can contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries

which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Pharmaceutical compositions of the invention can be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intraarterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, parenteral, topical, sublingual, or rectal means. Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Pharmaceutical preparations for oral use can be obtained through combination of active compounds with solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. suitable excipients are carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethylcellulose, or sodium carboxymethylcellulose; gums including arabic and tragacanth; and proteins such as gelatin and collagen. If desired, disintegrating or solubilizing agents can be added, such as the cross-linked polyvinyl pyrrolidone, agar, alginic acid, or a salt thereof, such as sodium alginate.

Dragee cores can be used in conjunction with suitable coatings, such as concentrated sugar solutions, which also can contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments can be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as

glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with a filler or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

Pharmaceutical formulations suitable for parenteral administration can be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection suspensions can contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds can be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Non-lipid polycationic amino polymers also can be used for delivery. Optionally, the suspension also can contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The pharmaceutical compositions of the present invention can be manufactured in a manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. The pharmaceutical composition can be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric, acetic, lactic, tartaric, malic, succinic, etc. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms. In other cases, the preferred preparation can be a lyophilized powder which can contain any or all of the following: 150 mM histidine, 0.1%2% sucrose, and 27% mannitol, at a pH range of 4.5 to 5.5, that is combined with buffer prior to use.

Further details on techniques for formulation and administration can be found in the latest edition of REMINGTON'S PHARMACEUTICAL SCIENCES (106). After pharmaceutical compositions have been prepared, they can be placed in an appropriate container and labeled for treatment of an indicated condition. Such labeling would include amount, frequency, and method of administration.

Material and Methods

One strategy for identifying genes that are involved in cardiovascular disease is to detect genes that are expressed differentially under conditions associated with the disease versus non-disease conditions. The sub-sections below describe a number of experimental systems which may be used to detect such differentially expressed genes. In general, these experimental systems include at least one experimental condition in which subjects or samples are treated in a manner associated with cardiovascular disease, in addition to at least one experimental control condition lacking such disease associated treatment. Differentially expressed genes are detected, as described below, by comparing the pattern of gene expression between the experimental and control conditions.

Once a particular gene has been identified through the use of one such experiment, its expression pattern may be further characterized by studying its expression in a different experiment and the findings may be validated by an independent technique. Such use of multiple experiments may be useful in distinguishing the roles and relative importance of particular genes in cardiovascular disease. A combined approach, comparing gene expression pattern in cells derived from CVD patients to those of *in vitro* cell culture models can give substantial hints on the pathways involved in development and/or progression of CVD.

Among the experiments which may be utilized for the identification of differentially expressed genes involved in arteriosclerosis, for example, are experiments designed

to analyze those genes which are involved in foam cell formation. Such experiments may serve to identify genes involved in the differentiation of this cell type, or their uptake of enzymatic modified LDL.

5 Within such an experiment, human blood is drawn and peripheral monocytes are isolated by methods routinely practiced in the art. These human monocytes can then be used immediately or cultured *in vitro*, using methods routinely practiced in the art, for 4 to 6 days where they develop more macrophage-like characteristics such as the up-regulation of scavenger receptors. These cells are then treated for various lengths
10 of time with agents thought to be involved in foam cell formation. These agents include but are not limited to enzymatic modified LDL and HDL. Control monocytes that are untreated or directly treated with native HDL are grown in parallel. At a certain time after addition of the test agents, the cells are harvested and analyzed for differential expression as described in detail below in the following section.

15 In order to identify differentially expressed genes, RNA, either total or mRNA, were isolated from one or more blood samples of the subjects utilized in experiments such as those described earlier. Total RNA samples were obtained from peripheral white blood cells (PWBC) of experimental subjects and from corresponding PWBC of
20 control subjects.

Below are methods described for the identification of genes which are involved in cardiovascular disease, including but not limited to arteriosclerosis, ischemia/reperfusion, hypertension, restenosis, and arterial inflammation. Such genes represent
25 genes which are differentially expressed in cardiovascular disease conditions relative to their expression in normal, or non-cardiovascular disease conditions or upon experimental manipulation based on clinical observations. Such differentially expressed genes represent "target" and/or "marker" genes. Methods for the further characterization of such differentially expressed genes, and for their identification as
30 target and/or marker genes, are presented below.

Thus, a differentially expressed gene may have its expression activated or completely inactivated in normal versus cardiovascular disease conditions (e.g., treated with enzymatic modified LDL versus untreated; mimicking of cholesterol efflux due to HDL treatment), or under control versus experimental conditions. Such a
5 qualitatively regulated gene will exhibit an expression pattern within a given tissue or cell type which is detectable in either control or cardiovascular disease subjects, but is not detectable in both.

Alternatively, a differentially expressed gene may have its expression modulated, i.e.,
10 quantitatively increased or decreased, in normal versus cardiovascular disease states, or under control versus experimental conditions. The degree to which expression differs in normal versus cardiovascular disease or control versus experimental states need only be large enough to be visualised via standard characterisation techniques, such as, for example, the differential display technique described below. Other such
15 standard characterisation techniques by which expression differences may be visualised include but are not limited to quantitative RT-PCR and Northern analyses, which are well known to those of skill in the art.

Physiological and biochemical significance of the results:

20

The Tables 1 and 2 show a summary of the genes, identified by the differential expression approach with DNA array technology and TaqMan analysis, which show an excellent correlation of gene expression levels.

25

All 74 nucleotide sequences were previously described in the literature but have not been previously recognised as being differentially expressed in CVD patients versus non-CVD patients.

30

Of these 74 nucleotide sequences, several are coding for transporter or channel proteins (e.g., voltage dependent anion channel1 (VDAC1), calmodulin like). These transporters can play an important role in the import and export of cholesterol or

- 90 -

triglycerides, one of the key steps in the generation of lipid vessels in macrophages, and if dysregulated, one step in direction of arteriosclerosis. The VDAC protein is thought to form the major pathway for movement of adenine nucleotides through the outer membrane and to be the mitochondrial binding site for hexokinase and glycerol kinase. And may also be involved in the signalling and initiation of an apoptotic cascade in the cell involving the BCL2 protein. The BCL2 family of proteins (see Bfl1), whose members may be anti-apoptotic or pro-apoptotic, regulates cell death by controlling this mitochondrial membrane permeability during apoptosis. Since macrophages transformed by high LDL load into foam cell are driven into apoptosis, within the so called fatty streaks, the upregulation of these genes can function as an indicative marker for arteriosclerosis. Some of the genes identified, belong to a signalling pathway system (e.g., epimorphin, lipoxin or G-CSFR). All represent receptors, mediating cell to cell interactions. Also isomerases and oxidoreductases show a tightly regulated expression pattern upon incubation with eLDL (e.g., IPP isomerase, 5-lipoxygenase, further see Table 4). These enzymes are involved in the degradation of fatty acids or in the synthesis of cholesterol. Some of the genes listed in the Tables 1 and 2 are involved in the phagosomal degradation of fatty acids (e.g., legumain or cathepsin L), which reflects the predispositional changes in the CVD patients analyzed. These genes were not directly affected by a mutation (in case of Tangier's Disease; ABCA1 transporter) but were differentially regulated upon comparison with the same gene in normal individual under the same eLDL conditions. So one can assume that these genes are good candidates for a diagnostic test or therapeutic interaction.

25

EXAMPLE 1Probe selection for the differential gene expression analysisProband and Patient Selection

5

For Expression analysis monocytes from healthy donors with Apo E3/E3 and E4/E4 genotype, as well as from Tangier's disease, familial hypercholestermia, Niemann Pick Type C and Lp(a) patients were isolated as described below. Probands and patients were identified and selected due to their clinical appearance and further genetic confirmation of the represented genotypes. For each group two individual were selected and expression profiles generated as described below. In total we have analysed RNA from 9 male and 9 female donors.

10

Monocyte Isolation and Cultivation

15

Human peripheral blood leukocytes from healthy normolipidemic volunteers were isolated by leukapheresis in a cell separator and subsequent counterflow centrifugation as described by Mueller et al; (107). To guarantee viability of the cells with minimal activation, isolated monocytes were cultured on Ultra Low Attachment Surfaces (Costar) in macrophage serum-free medium (Life Technologies) supplemented with monocyte colony-stimulating factor (M-CSF, 50 ng/ml) for up to 6 days. Cells were detached by rinsing the Costar Ultra Low Attachment Surfaces with PBS. For uptake experiments, 4-day cultured monocytes (10^6 cells per milliliter) were incubated with modified LDL for 2 hours at 37°C in 1 ml macrophage media containing 0.5% BSA.

20

25

Preparation of LDL

30

Human native LDL (1.006 mg/mL, density, 1.063 mg/ml) was isolated from the plasma of healthy blood donors by sequential preparative ultracentrifugation in KBr

gradients, followed by extensive dialysis and filter sterilization. Protein concentrations were determined by use of Lowry's method.

Chemical and Enzymatic Modification of LDL

5 Enzyme treatment was conducted with trypsin (6.6 mg/ml, Sigma) and cholesterol esterase (40 mg/ml, Roche Biochemica) for 6 to 8 hours at 37°C. Subsequently, the pH of the solution was adjusted to 5.5 by addition of MES buffer, pH 5.0. Finally, neuraminidase (79 mU/ml, Behring) and magnesium ascorbate solution (30 mg/ml)
10 were added for 14 hours at 37°C. The absence of oxidation products in E-LDL was verified by the determination of thiobarbituric acid-reactive substances to quantify lipid peroxidation products.¹² Modified lipoproteins were stored at 4°C and used within a week. During LDL preparation and subsequent modification, general precautions were taken to avoid LPS contamination. The latter was excluded by
15 *Limulus* endotoxin assay (Kinetic-QCL, BioWhittaker).

EXAMPLE 2

Differential DNA expression profiling

20 Expression profiling was carried out using the Affymetrix Array Technology. With minor modifications, the sample preparation protocol followed the Affymetrix GeneChip Expression Analysis Manual (Santa Clara, CA). Total RNA extraction and isolation from PWBC can be performed by using TRIzol (Life Technologies, Rockville, MD) and Oligotex mRNA Midi kit (Qiagen, Hilden, Germany), and an
25 ethanol precipitation step should be carried out to bring the concentration to 1 mg/ml. Using 5–10 mg of mRNA to create double stranded cDNA by the SuperScript system (Life Technologies). First strand cDNA synthesis was primed with a T7-(dT24) oligonucleotide. The cDNA can be extracted with phenol/chloroform and precipitated with ethanol to a final concentration of 1 mg /ml. From the generated cDNA,
30 cRNA can be synthesised using Enzo's (Enzo Diagnostics Inc., Farmingdale, NY) *in vitro* Transcription Kit. Within the same step the cRNA can be labelled with biotin

nucleotides Bio-11-CTP and Bio-16-UTP (Enzo Diagnostics Inc., Farmingdale, NY). After labelling and cleanup (Qiagen, Hilden (Germany)) the cRNA then should be fragmented in an appropriated fragmentation buffer (e.g., 40 mM Tris-Acetate, pH 8.1, 100 mM KOAc, 30 mM MgOAc, for 35 minutes at 94 °C). As per the Affymetrix protocol, fragmented cRNA should be hybridised on the HG_U95 array set (five chips A-E), comprising app. 13.000 probed transcripts each, for 24 hours at 60 rpm in a 45 °C hybridization oven. After Hybridization step the chip surfaces have to be washed and stained with streptavidin phycoerythrin (SAPE; Molecular Probes, Eugene, OR) in Affymetrix fluidics stations. To amplify staining, a second labeling step can be introduced, which is recommended but not compulsive. Here one should add SAPE solution twice with an antistreptavidin biotinylated antibody.

Hybridization to the probe arrays may be detected by fluorometric scanning (Hewlett Packard Gene Array Scanner; Hewlett Packard Corporation, Palo Alto, CA). After hybridization and scanning, the microarray images can be analyzed for quality control, looking for major chip defects or abnormalities in hybridization signal. Therefor either Affymetrix GeneChip MAS 4.0 Software or other microarray image analysis software can be utilized. Primary data analysis should be carried out by MAS Software.

In case of the genes analyses in one embodiment of this invention the primary data have been analysed by further bioinformatic tools and additional filter criteria. The bioinformatic analysis is described in detail below.

74 genes were identified to be at least 1.5 fold, differentially expressed in patients with cardiovascular disease in comparison to patients without cardiovascular disease. Due to the diversity of the group of cardiovascular disease patients, an inter group comparison was performed, to identify those genes and pathways that are involved in either differentiation and/or expressional reaction of macrophages under lipid stress (high eLDL environment). The differential expression of these 74 genes may only be observed in one group, (e.g. Tangier disease patients), due to the inherited mutation

in a specific gene in these patients and the resulting abnormal lipid trafficking. The specific regulation of these genes within one group compared to the others indicates their role in lipid trafficking and development of arteriosclerosis.

5 To confirm the results obtained by the array analysis with a second independent experimental approach, these 74 genes were analyzed by real-time quantitative PCR (TaqMan), using the PRISM 7700 Sequence Detection System of PE Applied Biosystems (Perkin Elmer, Foster City, CA, USA) with in the same cohort. Within
10 this technique a fluorogenic probe, consisting of an oligonucleotide labelled with both a fluorescent reporter dye and a quencher dye, is included in a typical PCR. Amplification of the probe-specific product causes cleavage of the probe, generating an increase in reporter fluorescence. Primers and probes were selected using the Primer Express software and localized mostly in the 3' region of the coding sequence or in the 3' untranslated region (see Table 3 for primer- and probe- sequences)
15 according to the positions of the probe sequence used for the construction of the Affymetrix HG_U95A-E chip. All primer pairs were checked for specificity by conventional PCR reactions. To standardise the amount of sample RNA, GAPDH was selected as a reference, since it was not differentially regulated in the samples analyzed. TaqMan validation experiments were performed showing that the
20 efficiencies of the target and the control amplifications are approximately equal which is a prerequisite for the relative quantitation of gene expression by the comparative $\Delta\Delta C_T$ method, known to those with skills in the art.

EXAMPLE 3

25

Data analysis

According to Affymetrix measurement technique (Affymetrix GeneChip Expression Analysis Manual, Santa Clara, CA) a single gene expression measurement on one
30 chip yields the average difference value and the absolute call. Each chip contains 16–20 oligonucleotide probe pairs per gene or cDNA clone. These probe pairs include

perfectly matched sets and mismatched sets, both of which are necessary for the calculation of the average difference, or expression value, a measure of the intensity difference for each probe pair, calculated by subtracting the intensity of the mismatch from the intensity of the perfect match. This takes into consideration variability in hybridization among probe pairs and other hybridization artefacts that could affect the fluorescence intensities. The average difference is a numeric value supposed to represent the expression value of that gene. The absolute call can take the values 'A' (absent), 'M' (marginal), or 'P' (present) and denotes the quality of a single hybridization. We used both the quantitative information given by the average difference and the qualitative information given by the absolute call to identify the genes which are differentially expressed in biological samples from individuals with cardiovascular disease versus biological samples from the normal population. With other algorithms than the Affymetrix one we have obtained different numerical values representing the same expression values and expression differences upon comparison.

The differential expression E in one of the cardiovascular disease groups compared to the normal population is calculated as follows. Given n average difference values d_1, d_2, \dots, d_n in the cardiovascular disease population and m average difference values c_1, c_2, \dots, c_m in the population of normal individuals, it is computed by the equation:

$$E \equiv \exp\left(\frac{1}{m} \sum_{i=1}^m \ln(c_i) - \frac{1}{n} \sum_{i=1}^n \ln(d_i)\right)$$

If $d_j < 50$ or $c_i < 50$ for one or more values of i and j , these particular values c_i and/or d_j are set to an "artificial" expression value of 50. These particular computation of E allows for a correct comparison to TaqMan results.

A gene is called up-regulated in cardiovascular disease versus normal if $E \geq 1.5$ and if the number of absolute calls equal to 'P' in the cardiovascular disease population is greater than $n/2$.

A gene is called down-regulated in cardiovascular disease versus normal if $E \leq 1.5$ and if the number of absolute calls equal to 'P' in the normal population is greater than $m/2$.

- 5 The final list of differentially regulated genes consists of all up-regulated and all down-regulated genes in biological samples from individuals with cardiovascular disease versus biological samples from the normal population. Those genes on this list which are interesting for a pharmaceutical application were finally validated by TaqMan. If a good correlation between the expression values/behavior of a transcript
- 10 could be observed with both techniques, such a gene is listed in Table 1 or 2.

TABLE 1

Genes which are up-regulated in diseased vs. Normal individuals

DNA Sequence	Protein Sequence	GB Acc	UNIGENE	LocusLink	Gene Name	Short Description of the Gene	Minimal Fold Change
SEQ ID NO. 37	SEQ ID NO.111	L32976	Hs.89449	4296	MLK-3 MLK3	HUMMLK3A protein kinase (MLK-3) mRNA, complete cds	7,0
SEQ ID NO. 6	SEQ ID NO.80	X13988	Hs.17384	4621	MYH3	mRNA for embryonic myosin heavy chain	5,0
SEQ ID NO. 70	SEQ ID NO.144	M98479	Hs.8265	7052	TGM2	tissue transglutaminase	5,0
SEQ ID NO. 60	Seq_ID134	U82812	Hs.522	922	CD5L	scavenger receptor cysteine rich Sp alpha mRNA, complete cds	4,0
SEQ ID NO. 72	SEQ ID NO.146	X03663	Hs.174142	1436	CSF1R	c-fms	4,0
SEQ ID NO. 65	SEQ ID NO.139	AF001383	Hs.193163	274	SH3P9 AMPHL	amphiphysin II mRNA, complete cds	3,5
SEQ ID NO. 9	SEQ ID NO.83	AB001325	Hs.234642	360	AQP3	AQP3 gene for aquaporine 3 (water channel), partial cds	3,0
SEQ ID NO. 11	SEQ ID NO.85	U61538	Hs.8531	11261	CHP	calcium-binding protein chp mRNA, complete cds	3,0
SEQ ID NO. 19	SEQ ID NO.93	Y08374	Hs.75184	1116	HTG; HTGS_PHAS	gene encoding cartilage GP-39 protein, exon 1 and 2 (and joined CDS)	3,0
SEQ ID NO. 33	SEQ ID NO.107	D17793	Hs.78183	8644	ets variant gene 6	mRNA for KIAA0119 gene, complete cds	3,0
SEQ ID NO. 42	SEQ ID NO.116	D14582	Hs.99865	2054	STX2C STX2B STX2A EPIM	mRNA for epimorphin	3,0
SEQ ID NO. 46	SEQ ID NO.120	AJ000414	Hs.73999	9322	TRIP10	mRNA for Cdc42-interacting protein 4 (CIP4)	3,0
SEQ ID NO. 48	SEQ ID NO.122	U48734	Hs.182485	81	ACTN4	non-muscle alpha-actinin mRNA,	3,0

DN Sequence	Protein Sequence	CB Acc	UNIGENE	LoeufLink	Gene Name	Short Description of the Gene	Minimal Fold Change
SEQ ID NO. 63	SEQ ID NO.137	H24861	Hs.117167			y142e11.r1 cDNA, 5 end	3,0
SEQ ID NO.74	SEQ ID NO.148	AF057557	Hs.58831	9214	TOSO	anti-Fas-induced apoptosis mRNA	3,0
SEQ ID NO. 13	SEQ ID NO.87	U22662	Hs.81336	10062	LXRA LXR-A	nuclear orphan receptor LXR-alpha mRNA, complete	2,5
SEQ ID NO. 55	SEQ ID NO.129	L26232	Hs.2837	5360	PLTP	phospholipid transfer protein mRNA, complete cds	2,5
SEQ ID NO. 7	SEQ ID NO.81	AB026833	Hs.241551	9635	CLCA2	mRNA for chloride channel protein, complete cds	2,0
SEQ ID NO. 17	SEQ ID NO.91	J04430	Hs.1211	54	ACP5	HUMACP5 tartrate-resistant acid phosphatase type 5	2,0
SEQ ID NO. 24	SEQ ID NO.98	X17025	Hs.7638	3422	IDI1	log of yeast IPP isomerase	2,0
SEQ ID NO. 26	SEQ ID NO.100	J03600	Hs.89499	240	LOX5 ALOX5	HUMLOX5 lipoxygenase mRNA, complete cds	2,0
SEQ ID NO. 35	SEQ ID NO.109	AF004709	Hs.178695	5603	SAPK4 PRKM13	stress-activated protein kinase 4 mRNA,	2,0
SEQ ID NO. 43	SEQ ID NO.117	M59818	Hs.2175	1441	G-CSFR-1 CSF3R	granulocyte colony-stimulating factor receptor (G-CSFR-1) mRNA, complete cds	2,0
SEQ ID NO. 59	SEQ ID NO.133	AL034562	Hs.156114	8194	1199_at PTPNS1	dJ684O24.2 (prodynorphin (Beta-Neoeendorphin-Dynorphin precursor, Proenkephalin B	2,0
SEQ ID NO. 64	SEQ ID NO.138	AF089750	Hs.179986	10211	FLOT1	flotillin-1 mRNA, complete cds	2,0
SEQ ID NO. 45	SEQ ID NO.119	AB006780	Hs.621	3958	GALBP MAC2	mRNA for galectin-3, complete cds	1,8
SEQ ID NO. 53	SEQ ID NO.127	U30930	Hs.15854	7368	UGT8	UDP-Galactose ceramide galactosyl transferase (CGT) mRNA	1,8

TABLE 2

Genes which are down-regulated in diseased vs. Normal individuals

DNA Sequence	Protein Sequence	GB_Acc	UNIGENE	LocusLink	Gene Name	Short Description of the gene	Minimal Fold Change
SEQ ID NO. 50	SEQ ID NO. 124	U03644	Hs.89421	9541		recepin mRNA, complete cds	- 6,0
SEQ ID NO. 61	SEQ ID NO. 135	X82460	Hs.77348	3248	HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	- 6,0
SEQ ID NO. 31	SEQ ID NO. 105	Y13647	Hs.119597	6319	SCD	mRNA for stearyl-CoA desaturase	- 5,0
SEQ ID NO. 56	SEQ ID NO. 130	U41387	Hs.169531	9188		Gu protein mRNA, partial cds	- 5,0
SEQ ID NO. 66	SEQ ID NO. 140	U69274	Hs.2861	27107		zinc finger protein mRNA, complete cds	- 5,0
SEQ ID NO. 73	SEQ ID NO. 147	S70154	Hs.278544	39	ACAT2	cytosolic acetoacetyl-coenzyme A thiolase, CT	- 5,0
SEQ ID NO. 28	SEQ ID NO. 102	U78294	Hs.111256		ALOX15B	15S-lipoxygenase mRNA, complete cds	- 4,0
SEQ ID NO. 44	SEQ ID NO. 118	U40572	Hs.172278	6645	SNT2B2	beta2-syntrophin (SNT B2) mRNA, complete cds	- 4,0
SEQ ID NO. 47	SEQ ID NO. 121	Z11793	Hs.3314	6414	SEPP1	mRNA for selenoprotein P	- 3,5
SEQ ID NO. 4	SEQ ID NO. 78	AF046873	Hs.125878	8224	SYN3	synapsin IIIa mRNA, complete cds	- 3,0
SEQ ID NO. 22	SEQ ID NO. 96	U27467	Hs.227817	597	Bfl-1 U2746 BCL2A1	HSU27467 Bcl-2 related (Bfl-1) mRNA, complete cds	- 3,0
SEQ ID NO. 25	SEQ ID NO. 99	AF061741	Hs.17144	9249	SDR1	retinal short-chain dehydrogenase reductase retSDR1 mRNA, complete cds	- 3,0
SEQ ID NO. 27	SEQ ID NO. 101	AB016247	Hs.28831	6309	C5D SC5DL	mRNA for sterol-C5-desaturase, complete cds	- 3,0

DNA Sequence	Protein Sequence	GB_Ace	UNIGENE	LocusLink	Gene Name	Short Description of the gene	Minimal Fold Change
SEQ ID NO. 49	SEQ ID NO.123	X68733	Hs.234726	12	ACT AACT	gene for alpha l-antichymotrypsin, exon 1	- 3,0
SEQ ID NO. 51	SEQ ID NO.125	Y09443	Hs.2258	8540	AGPS	mRNA for alkyl-dihydroxyacetonephosphate synthase precursor	- 3,0
SEQ ID NO. 58	SEQ ID NO.132	AB000220	Hs.171921	10512	IFN-alpha 6 SEMA3C	AB000220 mRNA for semaphorin E, complete cds	- 3,0
SEQ ID NO. 2	SEQ ID NO.76	U69108	Hs.29736	7188	U6910 TRAF5	HSU69108 TNF receptor associated factor 5 mRNA, partial cds	- 2,5
SEQ ID NO. 3	SEQ ID NO.77	L02320	Hs.25613	5962	RDX	radixin mRNA, complete cds	- 2,5
SEQ ID NO. 12	SEQ ID NO.86	AF026166	Hs.6456	10576	RBP-MS/type 4 CCT2	chaperonin-containing TCP-1 beta subunit log mRNA, complete cds	- 2,5
SEQ ID NO. 14	SEQ ID NO.88	U22431	Hs.19754	3091	HIF-1 alpha U2243 HIF1A	HSU22431 hypoxia-inducible factor 1 alpha (HIF-1 alpha) mRNA, complete cds	- 2,5
SEQ ID NO. 18	SEQ ID NO.92	AB020645	Hs.239189	2744	KIAA0838 Hs.172839	mRNA for KIAA0838 protein, complete cds	- 2,5
SEQ ID NO. 34	Seq_ID108	Y12735	Hs.3818	8444	DYRK3	mRNA for protein kinase, Dyk3	- 2,5
SEQ ID NO. 36	SEQ ID NO.110	X60188	Hs.861	5595	ERK1 ERK1 PRKM3	HSEK1 ERK1 mRNA for protein serine threonine kinase	- 2,5
SEQ ID NO. 54	SEQ ID NO.128	Z35102	Hs.8724	11329	protein kinase C inhibitor NDR	HSPROKINX mRNA for Ndr protein kinase	- 2,5
SEQ ID NO. 69	SEQ ID NO.143	M80482	Hs.17414	5046	PACE4	subtilisin-like protein (PACE4)	- 2,5
SEQ ID NO. 5	SEQ ID NO.79	M59830	Hs.27442	3304		MHC class III HSP70-2 gene (HLA), complete cds	- 2,2
SEQ ID NO. 1	SEQ ID NO.75	X58965	Hs.275163	4831	nm23-H2	RNA for nm23-H2 gene	- 2,0

DNA Sequence	Protein Sequence	GB Acc	UNIGENT	LocustLink	Gene Name	Short Description of the gene	Minimal Fold Change
SEQ ID NO. 8	SEQ ID NO.82	AB008775	Hs.14624	366	AQP9	AQP9 mRNA for aquaporin 9, complete cds	- 2,0
SEQ ID NO. 15	SEQ ID NO.89	U51903	Hs.78993	10788	IQGAP2 U5190	HSU51903 RasGAP-related protein (IQGAP2) mRNA, complete cds	- 2,0
SEQ ID NO. 16	SEQ ID NO.90	AF056490	Hs.78746	5151	rac protein kinase-alpha PDE8A	cAMP-specific phosphodiesterase 8A (PDE8A) mRNA, partial cds	- 2,0
SEQ ID NO. 20	SEQ ID NO.94	D55696	Hs.1869	5641	PRSC1	mRNA for cysteine protease, complete cds	- 2,0
SEQ ID NO. 21	SEQ ID NO.95	X12451	Hs.7856	1514	CTSL	mRNA for pro-cathepsin L (major excreted protein MEP)	- 2,0
SEQ ID NO. 23	SEQ ID NO.97	S81221	Hs.93199	4047	LSS	lanosterol synthase [, fetal liver, mRNA Partial, 2637 nt]	- 2,0
SEQ ID NO. 29	SEQ ID NO.103	AL050118	Hs.184641	9415	DKFZp586C201 FADSD6	mRNA; cDNA DKFZp586C201 (from clone DKFZp586C201)	- 2,0
SEQ ID NO. 30	SEQ ID NO.104	AF034544	Hs.1186	1717	DHCR7	delta7-sterol reductase mRNA, complete cds	- 2,0
SEQ ID NO. 32	SEQ ID NO.106	X77094	Hs.196352	4689	NCF4	mRNA for p40phox	- 2,0
SEQ ID NO. 38	SEQ ID NO.112	X13916	Hs.89137	4035	LRP1	mRNA for LDL-receptor related protein	- 2,0
SEQ ID NO. 39	SEQ ID NO.113	W60864	Hs.9963	7305	TYROBP	zd27g05.s1 cDNA, 3 end	- 2,0
SEQ ID NO. 40	SEQ ID NO.114	X74039	Hs.179657	5329	PLAUR	mRNA for urokinase plasminogen activator receptor	- 2,0
SEQ ID NO. 57	SEQ ID NO.131	Y08136	Hs.42945	10924	ASM3A ASML3a	mRNA for ASM-like phosphodiesterase 3a	- 2,0
SEQ ID NO. 67	SEQ ID NO.141	U49392	Hs.76364	199	AIF1	allograft inflammatory factor-1 (AIF-1) mRNA, complete cds	- 2,0
SEQ ID NO. 68	-----	AF035284	Hs.12214	3992		clone 23716 mRNA sequence	- 2,0
SEQ ID NO. 41	SEQ ID NO.115	M84562	Hs.99855	2358	FPRL1	formyl peptide receptor-like receptor (FPRL1)	- 1,8

DNA Sequence	Protein Sequence	GB_Ace	UNIGENE	LocustLink	Gene_Name	Short Description of the gene	Minimal Fold Change
						mRNA, complete cds	
SEQ ID NO. 52	SEQ ID NO.126	M58597	Hs.2173	2526	FUT4	ELAM-1 ligand fucosyltransferase (ELFT) mRNA, complete cds	- 1,8
SEQ ID NO. 62	SEQ ID NO.136	S60099	Hs.64797	334	APPH	APPH amyloid precursor protein log [, placenta, mRNA, 3727 nt]	- 1,8
SEQ ID NO. 71	SEQ ID NO.145	D38048	Hs.11865	5695	PSMB/	proteasomal subunit Z	- 1,8
SEQ ID NO. 10	SEQ ID NO.84	L06132	Hs.149155	7416	VDAC1	voltage-dependent anion channel isoform 1 (VDAC) mRNA, complete cds	- 1,6

TABLE 3

CVD gene	5' primer	3' primer
L26232	CTGCGCAGGTTCGGAATCT	GGCCTGTAAATGGATCAGA
AF061741	ACAGCACCTGGGCACACAC	GTCCTGCTCACCCAGCAGA
U41387	TCCTTCCCTGAAATAAATACCTAAGG	GCAGGTGGCTGAGGAAACC
L00352	TCTGGATCGTTTGACGGGA	TCTCTCCGGACATCAGTGCA
AF056490	CGCCTAATGCACTTCACAGGT	AAATAGAGTAGACTTTTGGAAATTGAATTATAAA
U22662	TCTGTTTCTTGGCCGGATG	TGCCCTTCTCAGTCTGTTCCTCA
J036600	AAACACCATAGGGACCCATTCTAC	GATTGCTGTTGCTGCTTGG
Y09443	ATCCTTGCTAATGGAGGGAGC	CCTTAGCCATTGCTTCCGTA
Y12735	GCTAACTTAATGTCAGAAACCAATGG	ATACACATATGCATCTCTGGGCA
Y08136	GAATCTAAAGGGAGAGTCCATCTGG	TCCGGCTGCAAATCTTCAAT
AB026833	TTATTGACCTGGAAGCTGTAAAAGTAGA	TAGCCTGGCCCTGATCAAAG
AF004709	TGTCGGTTGGAGAACTAGCT	CTGCAGGCGATTCTCCAGAT
X74039	CCATGTGGAGATAGAGCCCC	GGCTACATGTCCAAGGTGGC
AB016247	TGATGTTTGAAGTTACAACCTGTAAATTTT	GGAGAAAGAGGAGGAATAAGATTTTAGAA
U03644	AAGGGAGACAAGGAAACGGG	CTCTATACAAAGTCTGTGCCATGGC
U78294	TCCAAGCCTCAAAGTGCCC	CCACGGCTGTAAACGCAAA
AB000220	GTATCTCTGCACCGCTGCC	CATCCCAGGCGCAATAAGG
AB000220	AAAAGCACAAAGCGAACCCC	CACAACCCACGCTGCA

CVD-gene	5' primer	3' primer
D17793	GCTGGAGGTGCTGGTAGCTG	TGTTGGTGCCTGCCCTTC
AL050118	ATTGCCCTTTCAGCTCTAGATCCC	CAGTTCAACACCGTGCACG
AF0374544	GGGCACTGCTGAGGAATGAT	CCGAACAACATCTGGCATTIT
AB016247	ACCAGCAAGGCTGACCTGTC	CTCAAATACATCAAGCACAGCCTTA
AF089747	CAGAAAGAGGAATAAAATGATTAAAGTGC	TCTCTGCCCTCTGATTACAGGGTT
K02268	GACCCGGAAACAGCGTATCA	ATCCGACCTCTGACCCCTGG
AF019562	AGCAACACCTCCCTATTCTGTTATTT	ACACGTCAATGCTGTAGGTTGT
U82812	CCTGCCCTCCTGCCAAG	GGGCTCAAATGCTGTAGGTTGT
AL034562	GCCACGATCACAATCTGCAG	AATCCCAGCCCCACTCAG
J04430	GCCGCTGACTTCTTTCACAAG	CCTCCAAGGACAATCCAGCA
M58597	CTCGGTGCTGGGAGGGT	GGTGTCCCTTGTCAAGAGCATG
S81221	CCCTGACTAACAGCCTCAGCA	TTGGCCTCGTCTTCACTTGG
AF046873	GCCTTTAAGTGACTAAGGAACAACATAG	TTGAGAGGCACAAATTGAAGTATTCA
U51903	CTGACCCCTCGGCCCTCTACTTT	TGGTGTGGTCTTCTCTGAGTGAA
S60099	GTCAAAAAGCCAGAAATTCCTC	TTCACATTTAATTCTGCTGTCTGA
AB008775	CTATGGCCGAGGGTGAAGAC	GTAGGAGGTGGGCACGTAGC
AJ000414	CCCTAATGCCAGTTCCAGCTT	AGCCCCAAATCAGGGACAC
M84562	CAGGATTTCCACTGGACCTTG	ACCCAAATTCGGGTTCCAC
AB001325	AAGAACGCCCTGGAGTCCTAC	TCGGCCTCGCTGATCTTG

Gene	5' primer	3' primer
M59830	CATAGGAAAATGATCAAACAAGCAA	GGATGAGCGTAAGGCAGTAAGAA
H24861	GACTTTTITAGACAGATCTTCATGACCTG	ACCCTGCAGACCTTTTGGTG
L06132	AGCCTCATAGCTGAAGTTGCCT	TCAATGGACATGCTCAGGGA
AF089750	CACAGCACACCAGTCCC	CCCTCGCATGGCCCA
U48734	AAACCCACCCCTAGTTTCCCT	CGCGAAGTGACAGCTTTGAC
X60188	TTCACTGAGAGGGTCCCATGA	GAACACACATTTTTCGGGAG
AF001383	TCCCATGCTTGAGCTTCCA	CTACCTGTCTCCATGGCTTGC
AB020645	GCCATCTTGGCCAGGATTAA	AAGGAACCTGAGGGACCCC
Y13647	CTGTCTGCTTGGAGTTTACATATCAAA	AACCCATTGGCCAGACAAAA
U69274	CTCTGTTTCGGGAGCGGAG	AGCTCGTCGTCTGTGGTGGT
D14582	CTCAGCCGGGAAGATTTC	CATTGATGATCCGGTCCCC
U61538	TCATGCAGACCGGTACAAC	GAAAGTGGTAGCCGATGAG
Z35102	GATTTTGGTGGTCCGAGG	TGCAACACAAATACAATCGGC
U40572	GCTGAGCTGGAATTGCCA	CGCAACCAACTGTTTTCACC
L02320	CCTGTGATCCTTTGATGGCTTT	CATCAGTAACTCTCCTAGGGAGCTAC
AL137751	CAACTTGAGGAGAAACCTTTACAATT	GGTGACAAATGAAACTCTGTCTCAGA
U69108	CTTCCCCCTGGAAGCTGCAC	ACCGTCAGCTCATGGCATC
X77094	CATGCCCTTATGAGACTACTAATGAAATT	GGTTCAGTGCCAAAACCTCTCTACA
U30930	TCCGCGCTAAGACTCGAGAC	AATATACATTTTGCATATCTTCTGTCCCTG

C/D gene	5' primer	3' primer
X13988	ACCCTGCCCTGCTCTGC	GCTAGCCCAGATACCTGTTTGAG
Y08374	CCACAACACACAGATTTGAGCTC	GATGCCTCACTATCCCCACAG
M80927	GGGTCTATTGTGCTCCGCTAAAA	GAAAGAAATGGAAGACGCTGAAC
AF077200	TCCCACTGTCAATCAAAGACCTAA	GCTGGGTTATCCTGTAAAGTAGCAATC
XM016472	CTCTCTGGATGCCCTTCCTGC	TTCTGGCTTCACTGGATCCC
L32976	CAGGACCTTCTTCACAAGATGACTT	CCCACCCTAATTGTAGTTTTTCAG
D55696	ACAGGCCGAGTGATGCTTG	CAGAAGTCCCCACGAAATGGT
X58965	GCGTGTGGACAACATCATCAA	GATCGACAGCACGTGGGAAT
AF026166	GAGGGTCCATAAGCCCCATGAC	GCAGATCGCCTGGGAGG
M59818	TTTAATGAGAAATAGAAACGTAAACTATGACC	AAGTAATATTGTTTTGAGAGATAAGTAAAGGAAA
Z11793	AGGTGTCCAGTGGCTCCG	TTAGGATGGCAGATCTCTTGCC
U49392	GAATTGGAACATTATTACAGCAGCC	CACTAGATTTCATCCTTTTACACG
U22431	GACTATCTGCAGTGCGTCCCTACAG	AACATTTGTAGCACTCTGGACGTT
U27467	CCCTCCAACCCACAGCC	AATATGCCCTAGAGTAGATGCTGCTGAA
AF035284	TGTGCATTGCAGGATGGTG	TGGCAACATCCGGCATAAC
X17025	GACACTTTGCCAAGGCTCTCC	CATCCTTTCCCGCCTACCTC
X13916	CAAAGACCGGAGAAACCATTG	ATCACCGTCCACCAGCTCA
X12451	TTGCAGAGGCGTGCTG	TGTACACCTGCTTCAAGATTCCA
X82460	GCTCCCCCTGTTTGACGACA	TTAGGGTTAACATTGTACTTGCTTCATT

CVD-gene	5' primer	3' primer
M80482	AGCTGGAGAGAAACCAGATGTTGTTATTGAATC	GCTCCCCCTGTTTGACGACA
M55153	TTAGCAGGACTCATGCCCG	ATCCAACATATGCCATGCTTTGA
M98479	AAGGACTTGGAGAGAAATCATGCTGTGCA	TCCAGGGCCCCCA
X82460	TGCACAGCAGCCGGTTATTGTGC	TTAGCAGGACTCATGCCCG
D38048	GCCAGCCACCCACTGATGCCA	CCAAACAATGGACACTTCCTGA
X03663	CCTCTGGGAGATCTTCTCACTTGGGCTG	AGAGCGACGTCTGGTCCTATG
S70154	AATAGGACCAATTCCAGCCATAAAGCAAGCT	AGTGGGTGTGGAGCCTTCC

TABLE 4

RGD Accession	Detailed Description	Enzyme Class	Biological Function	Subcellular
X58965		Metabolism		
U69108	Member of a family of proteins that interact with the cytoplasmic domain of oligomerized TNF receptors, binds the lymphotoxin beta receptor (LTBR)	activator of NF-kappa B		Cytoplasmic
L02320	Radixin, member of a family of proteins that link the cytoskeleton and the plasma membrane, thereby regulating cell adhesion and cortical morphogenesis	Anchor Protein Proteasome		Cytoskeletal
AF046873	Synapsin III, a synaptic vesicle protein, a member of a family of proteins that bind ATP and may regulate neurotransmitter release	ATPase	Hydrolase	Cytoplasmic
M59830	Member of the heat shock HSP70 family of molecular chaperones that are involved in protein folding, translocation, and assembly into complexes, inducible by heat shock	ATPase	Chaperones	
X13988	Skeletal muscle myosin heavy chain, member of a family of motor proteins that provide the force for muscle contraction, expressed only during embryogenesis	ATPase	Hydrolase	Cytoplasmic
AB026833	Calcium-sensitive chloride channel, contains five transmembrane domains and displays an outward rectifying conductance of anions, expressed in the lung, trachea, and mammary gland, may be involved in the pathogenesis of cystic fibrosis	Channel [passive transporter]	Transporter	Plasma membrane

CB Acc	Detailed Description	Enzyme Class	Biological Function	Subcellular
AB008775	Aquaporin 9, a water and urea channel expressed predominantly in leukocytes	Channel [passive transporter]	Transporter	Plasma membrane
AB001325	Aquaporin 3, a water channel, member of the MIP family of proteins involved in transport of water, glycerol and other small molecules	Channel [passive transporter]	Transporter	Plasma membrane
L06132	Voltage-dependent anion channel 1 (mitochondrial porin channel), a voltage-gated pore of the outer mitochondrial membrane, mediates apoptotic signals from Bcl2 and related proteins that lead to release of cytochrome c	Channel [passive transporter]	Transporter	Cytoplasmic
U61538	Calcium-binding protein with similarity to calcineurin B and calmodulin, binds the sodium-potassium exchanger NHE1, inhibits GTPase-stimulation of NHE1 activity when overexpressed	Channel [passive transporter]	Transporter	
AF026166	Beta subunit of the cytosolic chaperonin containing TCP-1 (CCT), assists in the proper folding of tubulin, actin and contractin, may also be required for the proper folding of Cyclin E	Chaperones		Cytoskeletal
U22662	Member of the nuclear receptor superfamily, forms a heterodimer with the retinoid receptor that makes it responsive to retinoic acid	DNA-binding protein		Nuclear
U22431	Basic helix-loop-helix transcription factor that contains a PAS domain, heterodimerizes with the Ah receptor nuclear translocator (ARNT) and mediates transcriptional responses to hypoxia and dioxin-signaling	DNA-binding protein	Transcription factor	Nuclear
U51903	Protein with GTPase activating domain, multiple-calmodulin binding domains, and actin binding domain, inhibits GTPase activity of Cdc42 and Rac1, which are members of the ras family of GTP binding proteins	GTPase activating protein	Inhibitor or repressor	Cytoskeletal
AF056490	cAMP-specific phosphodiesterase, expressed in testis, ovaries, small intestine, and colon	Hydrolase		

GB Acc	Detailed Description	Enzyme Class	Biological Function	Subcellular
J04430	Tartrate-resistant acid phosphatase (purple acid phosphatase, type-5 acid phosphatase), a binuclear, iron-containing phosphatase expressed in monocytes and induced upon monocyte differentiation	Hydrolase	Other phosphatase	
AB020645	Protein with strong similarity to rat GIs, mitochondrial glutaminase, which contains ankyrin (Ank) repeats that may mediate protein-protein interactions	Hydrolase		Mitochondrial
Y08374	Cartilage glycoprotein-39, has similarity to chitinases, expressed in rheumatoid arthritis cartilage and synovial cells	Hydrolase	Structural protein	Extracellular matrix (cuticle and basement membrane)
D55696	Legumain, a cysteine endoprotease that hydrolyzes asparaginyl bonds	Hydrolase	Protease (
X12451	Cathepsin L, a lysosomal cysteine (thiol) protease that cleaves collagen and elastin and is highly expressed in transformed cells	Hydrolase	Protease	Cytoplasmic
U27467	Hemopoietic-specific early-response BCL2-related protein, expression is induced by phorbol ester and inflammatory cytokines, may protect cells during inflammation, required for mitochondrial viability and function	Inhibitor or repressor		
S81221	Lanosterol synthase ((S)-2,3-epoxysqualene mutase), catalyzes the cyclization of (S)-2,3-oxidosqualene to form lanosterol during sterol biosynthesis	Isomerase		
X17025	Isopentenyl diphosphate:dimethylallyl diphosphate isomerase (IPP isomerase), catalyzes the interconversion of isopentenyl diphosphate and dimethylallyl diphosphate in isoprenoid synthesis	Isomerase		Cytoplasmic
AF061741	Short-chain dehydrogenase/reductase, reduces all-trans-retinal during bleached visual pigment regeneration, may function in non-photoreceptor retinol metabolism	Oxidoreductase		Plasma membrane

GB Acc	Detailed Description	Enzyme Class	Biological Function	subcellular
J03600	5-lipoxygenase, catalyzes the first two steps in the synthesis of leukotrienes, which are involved in allergic and inflammatory responses	Oxidoreductase		Cytoplasmic
AB016247	Protein with similarity to <i>S. cerevisiae</i> Erg3p, which is a sterol-C5-desaturase	Oxidoreductase		
U78294	Arachidonate 15-lipoxygenase, converts arachidonic acid to 15S-hydroperoxyeicosatetraenoic acid, poorly metabolizes linoleic acid	Oxidoreductase		
AL050118	Delta-6 desaturase, desaturates 18:2(n-6) and 18:3(n-3) to form 20:4(n-6) (arachidonic acid) and 22:6(n-3) (docosahexaenoic acid)	Oxidoreductase		Plasma membrane
AF034544	7-dehydrocholesterol reductase, removes the C7-8 double bond in 7-dehydrocholesterol; mutations in the corresponding gene cause Smith-Lemli-Opitz syndrome	Oxidoreductase		Cytoplasmic
Y13647	Stearoyl-coenzyme A desaturase, functions in the synthesis of unsaturated fatty acids; upregulated in esophageal and colonic carcinomas and hepatocellular adenoma	Oxidoreductase		
X77094	Component of the cytosolic nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase complex, which is required for the oxidative burst, expressed only in hematopoietic cells	Oxidoreductase		Cytoplasmic
D17793	3 alpha-hydroxysteroid dehydrogenase, oxidizes xenobiotic alicyclic alcohols and 3alpha- or 17beta-hydroxy-5beta-androstanes, activated on exposure to all-trans-retinoic acid, may function in control of cell growth and differentiation	Oxidoreductase Transformation related	Transformation related	
Y12735	Dual-specificity protein kinase	Protein kinase	Transferase	
AF004709	MAP kinase that is activated by stress and proinflammatory cytokines, phosphorylated by MKK6 (PRKMK6)	Protein kinase	Transferaseserine	
X60188	MAP kinase that is activated in response to growth factors	Protein kinase	Transferase	Nuclear

GB Acc	Detailed Description	Enzyme Class	Biological Function	Subcellular
L32976	Member of the mixed-lineage kinase family, has SH3 and leucine zipper domains	Protein kinase	Transferase	
X13916	Low density lipoprotein receptor-related protein (alpha-2-macroglobulin receptor), binds to apoE containing lipoproteins and mediates chylomicron remnant clearance from the plasma	Receptor (protein translocation)		Plasma membrane
W60864	Protein with an immunoreceptor tyrosine-based activation motif (ITAM), associates with membrane glycoproteins of the killer-cell inhibitory receptor (KIR) family and activates NK cells	Receptor (signalling)		Plasma membrane
X74039	Urokinase-type plasminogen activator receptor, a member of a superfamily that includes CD59, murine Ly-6, and elapid snake venom toxins, functions in pericellular plasminogen activation	Receptor (signalling)		Plasma membrane
M84562	Lipoxin A4 receptor, a G protein-coupled receptor with similarity to the formyl peptide receptor (FPR1) that binds lipoxins and signals through an inhibitory G-protein to mobilize calcium, stimulates chemotaxis and cell adhesion	Receptor (signalling)		Plasma membrane
D14582	Epimorphin, a signaling protein, has strong similarity to murine Epim and rat Rn.10623; Epim functions in epithelial-mesenchymal interactions, Rn.10623 is involved in docking synaptic vesicles with the presynaptic plasma membrane	Receptor (signalling)		Plasma membrane
M59818	Granulocyte colony-stimulating factor receptor; mutation of the corresponding gene causes severe congenital neutropenia and is also associated with acute myeloid leukemia	Receptor (signalling)		Plasma membrane
U40572	Beta 2-syntrophin, an intracellular membrane-associated protein that binds to dystrophin (DMD), and utrophin/dystrophin related protein	Small molecule-binding protein		Basement membrane (extracellular matrix)

GB_Acc	Detailed Description	Enzyme Class	Biological Function	Subcellular
AB006780	Galectin 3, a lactose-binding lectin, involved in cell growth regulation	Small molecule-binding protein		Apical plasma membrane
AJ000414	Protein with an SH3 domain and similarity to the non-kinase domains of FER and Fes/Fps tyrosine kinases, binds to activated Cdc42 and may have a role in regulation of the actin cytoskeleton	Small molecule-binding protein CIP4 is a target for the small GTPase Cdc42		
Z11793	Selenoprotein that contains 10 selenocysteine residues, may function in antioxidant activities	Small molecule-binding protein - Undefined		
U48734	Alpha-actinin, a non-muscle cell actin-binding protein; localization to nucleus in cancer cells is correlated with good prognosis for breast cancer patients	Structural protein		Nuclear
X68733	Alpha-1-antichymotrypsin, a member of the serpin family of serine protease inhibitors; deficiency is associated with lung and liver disease	Structural protein pre-B cell colony enhancement	pre-B cell colony enhancement	
U03644	CBF1-interacting corepressor, links CBF1 and the histone deacetylase complex, binds to histone deacetylase and to SAP30	Transcription factor		
Y09443	Alkyl-dihydroxyacetonephosphate synthase, functions in ether phospholipid biosynthesis, may be deficient in peroxisomal biogenesis disorders Zellweger syndrome, rhizomelic chondrodysplasia punctata, and adrenoleukodystrophy	Transferase		Peroxisome
M58597	Myeloid alpha(1,3)fucosyltransferase (GDP-fucose:[Gal beta 1-4]GlcNAc alpha 1-3-fucosyltransferase), makes the 3-fucosyllactosamine epitope (CD15) on polymorphonuclear cells and monocytes, regulates Lex and Ley antigen expression	Transferase		Unspecified membrane
U30930	UDP-galactose ceramide galactosyltransferase, member of the UDP-glucuronosyltransferase 8 family of endoplasmic reticulum glycoproteins that is involved in synthesizing glycosphingolipids, cerebroside and sulfatides, myelin membrane constituents	Transferase		Endoplasmic reticulum

GB_Acc	Detailed Description	Enzyme Class	Biological Function	subcellular
Z35102	Serine/threonine kinase that localizes to the nucleus and is activated via autophosphorylation, expression is ubiquitous	Transferase		Nuclear
L26232	Phospholipid transfer protein, has roles in phospholipid transport and conversion of high density lipoproteins into larger and smaller particles	Transporter		
U41387				
Y08136	Protein of unknown function, has low similarity to a region of acid sphingomyelinases			
AB000220	Semaphorin E, member of a family of proteins involved in neuronal growth cone guidance and immune system regulation, overexpression is associated with resistance to the anticancer drug cis-diamminedichloroplatinum(II), associated with rheumatoid arthritis			
AL034562	Glycosylated receptor-like protein with three immunoglobulin-like domains that probably interacts with phosphotyrosine phosphatases, may have a role in response to growth factors and in cell adhesion			Plasma membrane
U82812	Spalpa, a member of the scavenger receptor cysteine-rich family that is expressed in lymphoid tissues and may be involved in the regulation of monocyte activation, function, and survival			Extracellular (excluding cell wall)
AL034562	Glycosylated receptor-like protein with three immunoglobulin-like domains that probably interacts with phosphotyrosine phosphatases, may have a role in response to growth factors and in cell adhesion			Plasma membrane
S60099				
H24861				
AF089750	Protein with very strong similarity to murine Mm.2931 (flotillin), which is an integral membrane protein of caveolae that is expressed in brain			Plasma membrane

GB Acc	Detailed Description	Enzyme Class	Biological Function	Subcellular
AF001383	Amphiphysin II, a tumor suppressor that interacts with MYC and colocalizes with ankyrin3 (ANK3), may have a role in endocytosis			Cytoplasmic
U69274				
U49392	Allograft inflammatory factor 1, cytokine inducible protein associated with vascular injury			Nuclear
AF035284				

CLAIMS

1. A method for the prediction, diagnosis or prognosis of a cardiovascular
5 disease by the detection of:
- a) a polynucleotide comprising at least one of the sequences of SEQ ID
NO. 1 to 74;
 - 10 b) a polynucleotide which hybridises under stringent conditions to a
polynucleotide specified in (a) and encodes a polypeptide exhibiting
the same biological function as specified for the respective sequence
in the Tables 1 and 2;
 - 15 c) a polynucleotide the sequence of which deviates from the poly-
nucleotide specified in (a) and (b) due to the generation of the genetic
code and encodes a polypeptide exhibiting the same biological
function as specified for the respective sequence in the Tables 1 and 2;
 - 20 d) a polynucleotide which represents a specific fragment, derivative or
allelic variation of a polynucleotide sequence specified in (a) to (c)
and encodes a polypeptide exhibiting the same biological function as
specified for the respective sequence in the Tables 1 and 2;
- 25 in a biological sample comprising the following steps:
- hybridising at least one polynucleotide specified in (a) to (d) to a nucleic
acid material of a biological sample, thereby forming a hybridization
complex; and
- 30 detecting said hybridization complex.

2. The method of claim 1, wherein before hybridization, the nucleic acid material of the biological sample is amplified.
- 5 3. A method for the prediction, diagnosis or prognosis of a cardiovascular disease by the detection of:
- 10 a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
- b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 15 c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 20 d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 25 e) a polypeptide encoded by a polynucleotide sequence specified in (a) to (d) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 30 f) a purified polypeptide comprising at least one of the sequences of SEQ ID NO. 75 to 147;

comprising the step of contacting a biological sample with a reagent which specifically interacts with the polynucleotide specified in (a) to (d) or the polypeptide specified in (e) and (f).

5

4. A diagnostic kit for conducting the method of any of claims 1 to 3.
5. A composition for the prediction, diagnosis or prognosis of cardiovascular disease comprising a detection agent for:

10

a) any polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;

15

b) any polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

20

c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

25

d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

30

e) a polypeptide encoded by a polynucleotide sequence specified in (a) to (d);

- f) a polypeptide comprising at least one of the sequences of SEQ ID NO. 75 to 147.
- 5 6. An array comprising a plurality of polynucleotides wherein each of the polynucleotides is selected from:
- a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
- 10 b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 15 c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 20 d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c);
- attached to a solid support.
- 25 7. A method of screening for agents which regulate the activity of a polypeptide encoded by a polynucleotide selected from the group consisting of:
- a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;

- b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

5

- c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

10

- d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

15

comprising the steps of:

contacting a test compound with at least one polypeptide encoded by a polynucleotide specified in (a) to (d); and

20

detecting binding of the test compound to the polypeptide, wherein a test compound which binds to the polypeptide is identified as a potential therapeutic agent for modulating the activity of the polypeptide in order to prevent or treat a cardiovascular disease.

25

8. A method of screening for agents which regulate the activity of a polypeptide encoded by a polynucleotide selected from the group consisting of:

- a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;

30

b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

5

c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

10

d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

15

comprising the steps of:

contacting a test compound with at least one polypeptide encoded by a polynucleotide specified in (a) to (d); and

20

detecting the activity of the polypeptide as specified for the respective sequence in the Tables 1 and 2, wherein a test compound which increases the activity is identified as a potential preventive or therapeutic agent for increasing the activity in a cardiovascular disease, and wherein a test compound which decreases the activity of the polypeptide is identified as a potential therapeutic agent for decreasing the activity in a cardiovascular disease.

25

30

9. A method of screening for agents which regulate the activity of a polynucleotide selected from group consisting of;

- 122 -

- 5
- a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
- b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 10
- c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 15
- d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;

20

comprising the steps of:

contacting a test compound with at least one polynucleotide specified in (a) to (d), and

25

detecting binding of the test compound to the polynucleotide, wherein a test compound which binds to the polynucleotide is identified as a potential preventive or therapeutic agent for regulating the activity of the polynucleotide in a cardiovascular disease.

30

10. Use of

- 5
- 10
- 15
- 20
- 25
- 30
- a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
 - b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
 - c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
 - d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c);
 - e) an antisense molecule targeting one of the polynucleotide sequences specified in (a) to (d);
 - f) a purified polypeptide encoded by a polynucleotide sequence specified in (a) to (d)
 - g) a purified polypeptide comprising at least one of the sequences of SEQ ID NO. 75 to 147;
 - h) an antibody capable of binding to one of the polynucleotide specified in (a) to (d) or a polypeptide specified in (f) and (g)
 - i) a reagent identified by any of the methods of claim 7 to 9 that modulates the amount or activity of a polynucleotide sequence specified in (a) to (d) or a polypeptide specified in (f) and (g)

for the preparation of compositions for the prevention, prediction, diagnosis, prognosis or a medicament for the treatment of a cardiovascular disease.

- 5 11. Use of claim 10 wherein the disease is atherosclerosis.
12. A reagent that regulates the activity of a polynucleotide selected from the group consisting of:
- 10 a) a polynucleotide comprising at least one of the sequences of SEQ ID NO. 1 to 74;
- 15 b) a polynucleotide which hybridises under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 20 c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 25 d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) and encodes a polypeptide exhibiting the same biological function as specified for the respective sequence in the Tables 1 and 2;
- 30 e) or a polypeptide encoded by at least one of the polynucleotides specified in (a) to (d);

wherein said reagent is identified by the method of any of the claims 7 to 9.

13. A pharmaceutical composition, comprising:

an expression vector containing at least one polynucleotide selected from the
group consisting of:

a) a polynucleotide comprising at least one of the sequences of SEQ ID
NO. 1 to 74;

b) a polynucleotide which hybridises under stringent conditions to a
polynucleotide specified in (a) encoding a polypeptide exhibiting the
same biological function as specified for the respective sequence in
the Tables 1 and 2;

c) a polynucleotide the sequence of which deviates from the poly-
nucleotide specified in (a) and (b) due to the generation of the genetic
code and encodes a polypeptide exhibiting the same biological
function as specified for the respective sequence in the Tables 1 and 2;

d) a polynucleotide which represents a specific fragment, derivative or
allelic variation of a polynucleotide sequence specified in (a) to (c)
and encodes a polypeptide exhibiting the same biological function as
specified for the respective sequence in the Tables 1 and 2;

or the reagent of claim 12 and a pharmaceutically acceptable carrier.

14. A computer-readable medium comprising at least one digitally encoded value
representing a level of expression of at least one polynucleotide sequence of
SEQ ID NO. 1 to 74 in a cell from the a subject at risk for or having
cardiovascular disease.

REFERENCES:**Patents cited:**

- U.S. Pat. No. 4,843,155
U.S. Pat. No. 5,262,31
5 1993
U.S. Pat. No. 4,683,202
U.S. Pat. No. 5,593,839
U.S. Pat. No. 5,578,832
U.S. Pat. No. 5,556,752
10 U.S. Pat. No. 5,631,734
U.S. Pat. No. 5,599,695
U.S. Pat. No. 4,683,195
U.S. Pat. No. 5,498,531
U.S. Pat. No. 5,714,331
15 U.S. Pat. No. 5,641,673
U.S. Pat. No. 5,565,332
U.S. Pat. No. 5,223,409
U.S. Pat. No. 5,705,151
U.S. Pat. No. 5,976,813
20 U.S. Pat. No. 5,283,317
- PCT No. WO 97/29212
PCT No. WO 97/27317
25 PCT No. WO 95/22058
PCT No. WO 99/12826
PCT No. WO 97/02357
PCT No. WO 93/03151
PCT No. WO 94/13804
30 PCT No. WO 94/10300
- Chomczynski, P.
Liang, P., and Pardee, A. B.,

Mullis, K. B., 1987

Haseloff et al.,

Lander, E. ,

Beutel et al.

EP No. 0 785 280

EP No. 0 799 897

EP No. 0 728 520

EP No. 0 721 016

5 EP No. 0 321 201

GB2188638B

Publications cited:

- 10 (1) Ross et al., Nature, 362, 801-809 (1993)
(2) Lusis et al., Nature, 407, 233-241 (2000)
(3) Sambrook et al., MOLECULAR CLONING: A LABORATORY MANUAL, 2d ed.,
(1989)
(4) Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley &
15 Sons, New York, N.Y., (1989).
(5) Tedder, T. F. et al., Proc. Natl. Acad. Sci. U.S.A. 85:208-212, (1988)
(6) Hedrick, S. M. et al., Nature 308:149-153, (1984)
(7) Lee, S. W. et al., Proc. Natl. Acad. Sci. U.S.A. 88:4225, (1984)
(8) Sarkar, PCR Methods Applic. 2, 318-322, (1993)
20 (9) Triglia et al., Nucleic Acids Res. 16, 81-86, (1988)
(10) Lagerstrom et al., PCR Methods Applic. 1, 111-119, (1991)
(11) Parker et al., Nucleic Acids Res. 19, 3055-3060, (1991)
(12) Copeland & Jenkins, Trends in Genetics 7: 113-118, (1991)
(13) Cohen, et al., Nature 366: 698-701, (1993)
25 (14) Bonner et al., J. Mol. Biol. 81, 123 (1973)
(15) Bolton and McCarthy, Proc. Natl. Acad. Sci. U.S.A. 48, 1390 (1962)
(16) Plump et al., Cell 71: 343-353, (1992)
(17) Van Heeke & Schuster, J. Biol. Chem. 264, 5503-5509, (1989)
(18) Grant et al., Methods Enzymol. 153, 516-544, (1987)
30 (19) Takamatsu, EMBO J. 6, 307-311, (1987)
(20) Coruzzi et al., EMBO J. 3, 1671-1680, (1984)

- (21) Broglie et al., Science 224, 838-843, (1984)
- (22) Winter et al., Results Probl. Cell Differ. 17, 85-105, (1991)
- (23) MCGRAW HILL YEARBOOK OF SCIENCE AND TECHNOLOGY, McGraw Hill, New York, N.Y., pp. 191-196, (1992)
- 5 (24) Engelhard et al., Proc. Nat. Acad. Sci. 91, 3224-3227, (1994)
- (25) Logan & Shenk, Proc. Natl. Acad. Sci. 81, 3655-3659, (1984)
- (26) Scharf et al., Results Probl. Cell Differ. 20, 125-162, (1994)
- (27) Freshney R.I., ed., ANIMAL CELL CULTURE , (1986)
- (28) Wigler et al., Cell 11, 223-232, (1977)
- 10 (29) Lowy et al., Cell 22, 817-823, (1980)
- (30) Wigler et al., Proc. Natl. Acad. Sci. 77, 3567-3570, (1980)
- (31) Colbere-Garapin et al., J. Mol. Biol. 150, 114, (1981)
- (32) Hartman & Mulligan, Proc. Natl. Acad. Sci. 85, 8047-8051, (1988)
- (33) Rhodes et al., Methods Mol. Biol. 55, 121-131, (1995)
- 15 (34) Hampton et al., SEROLOGICAL METHODS: A LABORATORY MANUAL, APS Press, St. Paul, Minn., (1990)
- (35) Maddox et al., J. Exp. Med. 158, 1211-1216, (1983)
- (36) Porath et al., Prot. Exp. Purif. 3, 263-281, (1992)
- (37) Kroll et al., DNA Cell Biol. 12, 441-453, (1993)
- 20 (38) Caruthers et al., Nucl. Acids Res. Symp. Ser. 215-223, (1980)
- (39) Horn et al. Nucl. Acids Res. Symp. Ser. 225-232, (1980)
- (40) Merrifield, J. Am. Chem. Soc. 85, 2149-2154, (1963)
- (41) Roberge et al., Science 269, 202-204, (1995)
- (42) Creighton, PROTEINS: STRUCTURES AND MOLECULAR PRINCIPLES, WH and
- 25 Co., New York, N.Y., (1983)
- (43) Cronin et al., Human Mutation 7:244, (1996)
- (44) Landegran et al., Science 241:1077-1080, (1988)
- (45) Nakazawa et al., PNAS 91:360-364, (1994)
- (46) Abravaya et al., Nuc Acid Res 23:675-682, (1995)
- 30 (47) Guatelli, J.C. et al., Proc. Natl. Acad. Sci. USA 87:1874-1878, (1990)
- (48) Kwoh, D.Y. et al., Proc. Natl. Acad. Sci. USA 86:1173 -1177, (1989)

- (49) Lizardi, P.M. *et al.*, Bio/Technology 6:1197, (1988)
- (50) Brown, Meth. Mol. Biol. 20, 18, (1994)
- (51) Sonveaux, Meth. Mol. Biol. 26, 1-72, (1994)
- (52) Uhlmann *et al.*, Chem. Rev. 90, 543-583, (1990)
- 5 (53) Gee *et al.*, in Huber & Carr, MOLECULAR AND IMMUNOLOGIC APPROACHES, Publishing Co., Mt. Kisco, N.Y., (1994)
- (54) Agrawal *et al.*, Trends Biotechnol. 10, 152-158, (1992)
- (55) Uhlmann *et al.*, Tetrahedron. Lett. 215, 3539-3542, (1987)
- (56) Cech, Science 236, 1532-1539, (1987)
- 10 (57) Cech, Ann. Rev. Biochem. 59, 543-568, (1990)
- (58) Couture & Stinchcomb, Trends Genet. 12, 510-515, (1996)
- (59) Haseloff *et al.* Nature 334, 585-591, (1988)
- (60) Kohler *et al.*, Nature 256, 495-497, (1985)
- (61) Kozbor *et al.*, J. Immunol. Methods 81, 3142, (1985)
- 15 (62) Cote *et al.*, Proc. Natl. Acad. Sci. 80, 2026-2030, (1983)
- (63) Cole *et al.*, Mol. Cell Biol. 62, 109-120, (1984)
- (64) Morrison *et al.*, Proc. Natl. Acad. Sci. 81, 6851-6855, (1984)
- (65) Neuberger *et al.*, Nature 312, 604-608, (1984)
- (66) Takeda *et al.*, Nature 314, 452-454, (1985)
- 20 (67) Burton, Proc. Natl. Acad. Sci. 88, 11120-11123, (1991)
- (68) Thirion *et al.*, Eur. J. Cancer Prev. 5, 507-11, (1996)
- (69) Coloma & Morrison, Nat. Biotechnol. 15, 159-63, (1997)
- (70) Mallender & Voss, J. Biol. Chem. 269, 199-206, (1994)
- (71) Verhaar *et al.*, Int. J. Cancer 61, 497-501, (1995)
- 25 (72) Nicholls *et al.*, J. Immunol. Meth. 165, 81-91, (1993)
- (73) Orlandi *et al.*, Proc. Natl. Acad. Sci. 86, 3833-3837, (1989)
- (74) Winter *et al.*, Nature 349, 293-299, (1991)
- (75) Lam, Anticancer Drug Des. 12, 145, (1997)
- (76) DeWitt *et al.*, Proc. Natl. Acad. Sci. U.S.A. 90, 6909, (1993)
- 30 (77) Erb *et al.* Proc. Natl. Acad. Sci. U.S.A. 91, 11422, (1994)
- (78) Zuckermann *et al.*, J. Med. Chem. 37, 2678, (1994)

- (79) Cho et al., Science 261, 1303, (1993)
- (80) Carell et al., Angew. Chem. Int. Ed. Engl. 33, 2059 & 2061, (1994)
- (81) Gallop et al., J. Med. Chem. 37, 1233, (1994)
- (82) Houghten, BioTechniques 13, 412-421, (1992)
- 5 (83) Lam, Nature 354, 8284, (1991)
- (84) Fodor, Nature 364, 555-556, (1993)
- (85) Cull et al., Proc. Natl. Acad. Sci. U.S.A. 89, 1865-1869, (1992)
- (86) Scott & Smith, Science 249, 386-390, (1990)
- (87) Devlin, Science 249, 404-406, (1990)
- 10 (88) Cwirla et al., Proc. Natl. Acad. Sci. 97, 6378-6382, (1990)
- (89) Felici, J. Mol. Biol. 222, 301-310, (1991)
- (90) Jayawickreme et al., Proc. Natl. Acad. Sci. U.S.A. 19, 1614-1618, (1994)
- (91) Chelsky, Strategies for Screening Combinatorial Libraries (1995)
- (92) Salmon et al., Molecular Diversity 2, 57-63, (1996)
- 15 (93) McConnell et al., Science 257, 1906-1912, (1992)
- (94) Sjolander & Urbaniczky, Anal. Chem. 63, 2338-2345, (1991)
- (95) Szabo et al., Curr. Opin. Struct. Biol. 5, 699-705, (1995)
- (96) Zervos et al., Cell 72, 223-232, (1993)
- (97) Madura et al., J. Biol. Chem. 268, 12046-12054, (1993)
- 20 (98) Bartel et al., BioTechniques 14, 920-924, (1993)
- (99) Iwabuchi et al., Oncogene 8, 1693-1696, (1993)
- (100) Findeis et al. Trends in Biotechnol. 11, 202-205, (1993)
- (101) Chiou et al., GENE THERAPEUTICS: METHODS AND APPLICATIONS OF DIRECT
GENE TRANSFER (J.A. Wolff, ed.), (1994)
- 25 (102) Wu & Wu, J. Biol. Chem. 263, 621-24, (1988)
- (103) Wu et al., J. Biol. Chem. 269, 542-46, (1994)
- (104) Zenke et al., Proc. Natl. Acad. Sci. U.S.A. 87, 3655-59, (1990)
- (105) Wu et al., J. Biol. Chem. 266, 338-42, (1991)
- (106) REMINGTON'S PHARMACEUTICAL SCIENCES (Maack Publishing Co., Easton,
30 Pa.
- (107) Muller et al., Arterioscler Thromb 13:1317-1326 (1993)

- (108) Needleman SB, Wunsch, J Mol Biol. 48, 443-53, 1970
- (109) Henikoff S, Henikoff JG, Proc. Natl. Acad. Sci. USA 89,10915-10919, 1992
- (110) Hille, Excitable Membranes, Sunderland, MA, Sinauer Associates, Inc.

- 1 -

SEQUENCE LISTING

<110> Bayer AG

<120> Genes and proteins for prevention, prediction, prognosis and therapy of cardiovascular disease

<130> Lea 35643 WO

<150> GB0124145

<151> 2001-10-08

<160> 147

<170> PatentIn version 3.1

<210> 1

<211> 670

<212> DNA

<213> Homo sapiens

<400> 1

cggccacgag goggaatccc ttctgctctc ccagcgcagc gccgcccgcc ggcccctcca	60
gcttcccgga ccatggccaa cctggagcgc accttcacgc ccatcaagcc ggacggcgtg	120
cagcgcggcc tgggtgggca gatcatcaag cgcttcgagc agaagggatt ccgcctcgtg	180
gccatgaagt tctccgggc ctctgaagaa cacctgaagc agcactacat tgacctgaaa	240
gaccgaccat tcttccttgg gctgggtgaag tacatgaact cagggccggt tgtggccatg	300
gtctgggagg ggctgaacgt ggtgaagaca ggccgagtga tgcttgggga gaccaatcca	360
gcagattcaa agccaggcac cattcgtggg gacttctgca ttcagggttg caggaacatc	420
attcatggca gtgattcagt aaaaagtgct gaaaaagaaa tcagcctatg gtttaagcct	480

- 2 -

gaagaactgg ttgactacaa gtcttgtgct catgactggg tctatgaata agaggtggac 540
 acaacagcag tctccttcag cacggcgtgg tgtgtccctg gacacagctc ttcattccat 600
 tgacttagag gcaacaggat tgatcattct tttatagagc atatttgcca ataaagcttt 660
 tggaagccgg 670

<210> 2

<211> 2738

<212> DNA

<213> Homo sapiens

<400> 2

ggcaactcca tttccttgga ctttgagccc agtatagagt accagtttgt ggagcgggtg 60
 gaagagcgct acaaattgtgc cttctgccac tcggtgcttc acaaccccca ccagacagga 120
 tgtgggcacc gcttctgcca gcactgcac ctgtccctga gagaattaaa cacagtgcc 180
 atctgccctg tagataaaga ggtcatcaaa tctcaggagg tttttaaaga caattgttgc 240
 aaaagagaag tcctcaactt atatgtatat tgcagcaatg ctctgggatg taatgccaag 300
 gttattctgg gcggtacca ggatcacctt cagcagtgtc tatttcaacc tgtgcagtgt 360
 tctaattgaga agtgccggga gccagtccta cggaaagacc tgaaagagca tttgagtgcg 420
 tcctgtcagt ttcgaaagga aaaatgcctt tattgcaaaa aggatgtggt agtcatcaat 480
 ctacagaatc atgaggaaaa cttgtgtcct gaataccagc tattttgtcc caacaattgt 540
 gcgaagatta ttctaaaaac tgaggtagat gaacacctgg ctgtatgtcc tgaagctgag 600
 caagactgtc cttttaagca ctatggctgt gctgtaacgg ataaacggag gaacctgcag 660
 caacatgagc attcagcctt acgggagcac atgcgttttg ttttagaaaa gaatgtccaa 720
 ttagaagaac agatttctga cttacacaag agcctagaac agaaagaaag taaaatccag 780
 cagctagcag aaactataaa gaaacttgaa aaggagttca agcagtttgc acagttgttt 840
 ggcaaaaatg gaagcttcct cccaaacatc caggtttttg ccagtcacat tgacaagtca 900
 gcttggctag aagctcaagt gcatcaatta ttacaaatgg ttaaccagca acaaaataaa 960
 tttgacctga gacctttgat ggaagcagtt gatacagtga aacagaaaat taccctgcta 1020
 gaaaacaatg atcaaagatt agccgtttta gaagaggaaa ctaacaaaca tgataccac 1080
 attaatatc ataaagcaca gctgagtaaa aatgaagagc gatttaaact gctggagggt 1140

- 3 -

acttgctata atggaaagct catttggaag gtgacagatt acaagatgaa gaagagagag	1200
gcggtggatg ggcacacagt gtccatcttc agccagtcct tctacaccag ccgctgtggc	1260
taccggctct gtgctagagc atacctgaat ggggatgggt cagggagggg gtcacacctg	1320
tccctatact ttgtgggtcat gcgaggagag ttgactcac tgttgcagtg gccattcagg	1380
cagaggggtga ccctgatgct tctggaccag agtggcaaaa agaacattat ggagaccttc	1440
aaacctgacc ccaatagcag cagctttaaa agacctgatg gggagatgaa cattgcatct	1500
ggctgtcccc gctttgtggc tcattctgtt ttggagaatg ccaagaacgc ctacattaaa	1560
gatgacactc tgttcttgaa agtggccgtg gacttaactg acctggagga tctctagtca	1620
ctgttatggg gtgataagag gacttcttgg ggccagaact ggaggagagc acatttgatt	1680
atcatattga cctggattta gactcaaage acatttgtat ttgccttttt ccttaacgtt	1740
tgaagtcagt ttaaaacttc tgaagtgtg tctttttaca tttactctg tcccagtttg	1800
aaacttaaaa ctcttagaat attctcttat tatttatatt tttatatattc ttgaaagatg	1860
gtaagtttct tgaagttttt ggggcgtttc tcttttactg gtgcttagcg cagtgtctcg	1920
ggcactctaa atattgagtg ttatggagga cacagaggta gcagaatccc agttgaaaat	1980
gttttgatat ttattgttt ggctattga ttctagacct ggcttaagt ctgcaaaagc	2040
catctttata aggtaggctg ttccagttaa gtagtgggtg atgtagttac aaagataata	2100
tgctcagttt ggaccttttt ttcagttaaa tgctaaatat atgaaaatta ctataacctc	2160
aagtattttc atgaaattca ccagcagttt gcaagcacag ttttgcaagg ctgcataaga	2220
actggtgaat ggggtaagca ttttcattct tcctgctgaa gtaaagcaga aagtactgca	2280
tagtatatga gatatagcca gctagctaaa gttcagattt tgttaggttc aaccctatga	2340
aaaaaactat tttcataggt caaaaatggg aaaaaattag cagtttcata agattcaacc	2400
aaataaatat atatatacac acacacatac atatacacct atatatgtgt gtatacaaac	2460
agttcgaaatg tattttgggtg acagtaataa atcaatgtga ggatggatag aatttagtat	2520
atgatagaga aaatgtcata aatggataaa aggaatttac aacttgagga gaaaaccttt	2580
acaatttcct atgggtgtca gaagtactct cagcgaaaac tgatggctaa aacagtatct	2640
actattctct gataactttt tttctgagac agagtttcat tgtcaccag gctggagtac	2700
agtggcatga tctcagctca ctgcaaactc tgctccc	2738

- 4 -

<210> 3

<211> 2022

<212> DNA

<213> Homo sapiens

<400> 3

aattcggcac	gagacaaaaa	gagaaagaaa	atgccgaaac	caatcaacgt	aagagtaact	60
acaatggatg	ctgagctgga	atttgccatt	cagcccaata	caactggcaa	acaacttttt	120
gaccaggtgg	tgaaaacagt	tggtttgcgt	gaggtctggt	tttttgggct	gcagtatgta	180
gacagcaaag	gttattctac	atggcttaaa	ctaaataaaa	aggtaacaca	gcaggatggt	240
aaaaaagaga	atcctttaca	gttcaagttt	agagctaaat	tctttcctga	agatgtttct	300
gaggaattaa	ttcaagaaat	aaccagaga	ctcttcttct	tgcaagttaa	agaagccatc	360
ttaaatgatg	agatatattg	cccgccagaa	actgcagttc	ttttggcttc	ctatgctgtc	420
caagccaagt	atggagatta	caataaagag	attcataagc	caggctacct	ggctaattgat	480
agactcctac	cccagcgtgt	attggaacaa	cacaaactaa	caaaagaaca	gtgggaagaa	540
agaatacaga	actggcatga	agaacataga	ggaatgttaa	gggaggattc	tatgatggaa	600
tacctgaaga	ttgcacaaga	tctagaaatg	tatggagtca	actattttga	aataaaaaat	660
aaaaaaggaa	ctgaattgtg	gctaggtgtt	gatgctttgg	gtctgaatat	ttatgagcat	720
gacgacaagt	taacacctaa	aattgggtttt	ccctggagtg	aatcagaaa	tatttcattt	780
aatgacaaaa	aatttgttat	aaagccaatc	gacaaaaagg	cacctgattt	tgtgttttat	840
gcacctcgtc	tgagaatcaa	taagcggatt	ttggccttat	gtatgggaaa	ccatgaacta	900
tacatgcgaa	gaaggaagcc	tgatactatt	gaagtacaac	agatgaaggc	tcaggctagg	960
gaggagaaac	atcagaagca	gttggaagg	gcacaattag	agaatgaaaa	gaagaaaaga	1020
gaaatagcag	aaaaggaaaa	ggaaagaata	gaacgtgaaa	aggaagagct	aatggaacgt	1080
ctaaaacaaa	ttgaagagca	gacaattaaa	gctcagaaag	aactagaaga	acagactcga	1140
aaagctctag	aactggatca	agaacgaaaa	cgagcaaaag	aagaagcaga	acgacttgaa	1200
aaggagcgtc	gagctgctga	agaggcaaag	tctgccatag	caaaacaagc	tgccgaccag	1260
atgaagaatc	aggagcagct	agcagcagaa	cttgctgaat	tactgccaa	gattgcactt	1320
ctagaggaag	ccaagaagaa	aaaggaagag	gaagcaactg	agtggcaaca	caaagctttt	1380
gcagcccagg	aagacttgga	aaagaccaa	gaagagttaa	aaactgtgat	gtctgcccc	1440

- 5 -

cctccacctc caccaccacc agtcattcct ccaacagaaa acgaacatga tgaacacgat 1500
 gagaataatg ctgaagctag tgctgaatta tcaaatgaag gggtaatgaa ccatagaagc 1560
 gaggaagaac gtgtaaccga aacacagaaa aatgagcgtg ttaagaagca acttcaggca 1620
 ttaagttcag aattagccca agccagagat gaaaccaaga aaacacaaaa tgatgttctt 1680
 catgctgaga atgttaaagc aggccgtgat aagtacaaga ctctgcgaca gattcgacaa 1740
 ggcaatacaa agcagcgtat cgatgagttt gaagcaatgt gagagctggt attttgcata 1800
 tatgttcttc ataagctgaa ccaccaacag agaaaagcag gcctttgcag atatgatgga 1860
 atgcatccca ccttgccaaa gcacttacac cagtttgact gtgctagcta aaagacaaat 1920
 ttaaggggag ctcttcaaca ttaaggcagt atgatatcat gcttggtttt cttttttctt 1980
 ttggtccagg gaatggagaa tgggtgttcca ttgcctcttt tt 2022

<210> 4

<211> 2152

<212> DNA

<213> Homo sapiens

<400> 4

tgggtaggag ccagtcattc ccatccatcc acagccatga atttctccg ggcagctctc 60
 tctgacagca gcttcatggc caacctgcct aatggctata tgacggacct gcaacgacca 120
 gatagctoca ccagctcacc tgcttcccc gccatggaga ggaggcacc ccagccctg 180
 gctgcctcct tctcctctcc aggatccagc ctttttagct ccctctccag tgccatgaag 240
 caggccctc aggcacctc aggactgatg gagcctccag gtccctccac gccattggt 300
 caaagacca ggatcctggt ggtgatcgat gatgccata cagactggtc gaagtatttc 360
 catgggaaga aggtgaatgg agagattgag atccgagtgg agcaggctga attctcagag 420
 ttgaacctag ctgcctatgt gaccgggggc tgcattggtg acatgcaggt cgtgagaaat 480
 gggaccaaag tggtagcag atccttcaag ccagacttca tcctgggtccg ccagcatgcc 540
 tacagcatgg ccctggggga agactaccgc agcctggtea tcggcctgca gtatggaggg 600
 ctgcctgctg tcaactctct ctactccgct tacaacttct gcagcaagcc ctgggtgttc 660
 tctcagctca ttaagatctt ccattccctg ggtcctgaga agttcccgct tgtggagcaa 720
 acatttttcc ccaaccataa gccaatggtc acagcccccac acttcccggt ggtagtcaag 780

- 6 -

```

ctgggacatg cccacgctgg aatgggaaag atcaaagtgg aaaaccagct tgacttccag      840
gacatcacca gcgtggctgc catggccaaa acatacgcca ccaccgaggc gttcatcgac      900
tccaagtacg acatccgcat ccagaaaatt ggatccaact acaaggctta catgagaacc      960
tccatctctg ggaactggaa ggccaacaca ggctctgcca tgctggagca ggtggccatg     1020
acagagaggt acaggctgtg ggtggacagc tgctcgaaa tgtttggcgg cctggacatc     1080
tgtgccgtca aggctgtcca cagcaaggat ggcagagatt acatcatcga ggtaatggac     1140
agctcaatgc cgctgattgg agagcatgtg gaagaggaca gacagctgat ggccgacctt     1200
gttgtctcca aatgagcca gctcccgatg ccaggaggca cagcgccctc cccctcaga      1260
ccttgggctc cacagattaa atcagcgaaa tcccaggggc aagcccagct ggggcctcag      1320
ctaggccagc cccagccacg cccacctcg caaggaggcc ctcgccaage tcagtctcct      1380
cagccccaga gatctggaag cccctcccaa cagaggctct cccacaagg ccagcagccc      1440
ctgagcccc agtcgggatc tccacagcag caaaggctac caggctctcc gcagctatcc      1500
cgggcatcca gtggcagctc cccaaaccag gcctccaage caggtgccac cctcgctca      1560
cagccccggc cccctgtgca gggccgtagt acctcccagc aggggtgaaga gtccaagaag      1620
ccagcaccac cccatccgca tctcaacaaa tctcagtccc tgactaacag cctcagcaca      1680
tccgacacct cccagcgtgg gaccccaagt gaagacgagg ccaaggctga aaccatccgc      1740
aacctgagga agtcttttgc cagcctgttc tctgactaac gccatccagg ctgggagggg      1800
aagagtgcta tggtaactc gtccccctcc tgctcatct tecttctcag ccttggttcc      1860
tgatgggaac agaatggagg gcctgagaac atactttcta aatgcctttg acccaggaac      1920
cgattatcta tatttggttc cattttcctt caccgtgaca ttccagcatt gtctgactgt      1980
gaggtgggccc tttgagagcc tccaggttcc tcaaaacagg cctgagcgat gggcatcaca      2040
ccctctgcct acccacgtgc atgcttacct gccagataac caagtgagat gtctgcgagt      2100
ggctagtttt cacattctta ctagtgtttg gctcaccttt gggcaaaggc cc              2152

```

<210> 5

<211> 2876

<212> DNA

<213> Homo sapiens

<400> 5

```

tgccatgaga ccaacacct tcccaccacc actccccctt ctctcagggc cctgtcccc      60

```


tccagtgaat cccagaagac tctggagagt tctgagcaga gggcggcacc ctgccctctg	120
attggtccaa ggaaggctgg ggggcaggac gggaggcgaa acccctggaa tattcccgac	180
ctggcagcct catcgagctt ggtgattggc tcagaagggg aaaggcgggt ctccacgacg	240
acttataaaa gccgaggggc gcgcgggtccg gaaaacggcc agcctgagga gctgctgoga	300
gggtccgctt cgtctttcga gagtgactcc cgcgggtccca aggcctttcca gagcgaacct	360
gtgcggctgc aggcaccggc gtgttgagtt tccggcgctc cgaaggactg agctcttgtc	420
gcggatcccg tccgcggttt ccagcccccga gtctcagagc ggagcccaca gagcagggca	480
ccggcatggc caaagccgcg gcgatcggca tcgacctggg caccacctac tcctgcgtgg	540
gggtgttcca acacggcaag gtggagatca tcgccaacga ccagggcaac cgcaccaccc	600
ccagctacgt ggccttcacg gacaccgagc ggctcatcgg ggatgcggcc aagaaccagg	660
tggcgctgaa cccgcagaac accgtgtttg acgcgaagcg cctgatcggc cgcaagtctg	720
gcgacccggg ggtgcagtcg gacatgaagc actggccttt ccagggtgatc aacgacggag	780
acaagcccaa ggtgcaggtg agctacaagg gggagaccaa ggcattctac cccgaggaga	840
tctcgtccat ggtgctgacc aagatgaagg agatcgccga ggcgtacctg ggctaccggg	900
tgaccaacgc ggtgatcacc gtgccggcct acttcaacga ctgcgcagcg caggccacca	960
aggatgcggg tgtgatcgcg gggctcaacg tgctgcggat catcaacgag cccacggccg	1020
ccgccatcgc ctacggcctg gacagaacgg gcaaggggga gcgcaacgtc ctgatctttg	1080
acctgggcgg gggcaccttc gacgtgtcca tcctgacgat cgacgacggc atcttcgagg	1140
tgaaggccac ggccggggac acccacctgg gtggggagga ctttgacaac aggctggtga	1200
accacttcgt ggaggagttc aagagaaaac acaagaagga catcagccag aacaagcgag	1260
ccgtgaggcg gctgcgcacc gcctgcgaga gggccaagag gaccctgtcg tccagcacc	1320
aggccagcct ggagatcgac tcctgtttg agggcatcga cttctacacg tccatcacca	1380
gggcgaggtt cgaggagctg tgctccgacc tgttccgaag caccctggag cccgtggaga	1440
aggctctgcg cgacgccaag ctggacaagg ccagattca cgacctggtc ctggtcgggg	1500
gctccacccg catccccaa gtcgagaagc tgctgcaaga cttcttcaac gggcgcgacc	1560
tgaacaagag catcaacccc gacgaggctg tggcctacgg ggcggcgggtg caggcggcca	1620
tcctgatggg ggacaagtcc gagaacgtgc aggacctgct gctgctggac gtggctcccc	1680
tgctcgtggg gctggagacg gccggaggcg tgatgactgc cctgatcaag cgcaactcca	1740
ccatccccac caagcagacg cagatcttca ccacctactc cgacaaccaa cccgggggtgc	1800

- 8 -

tgatccaggt gtacgagggc gagagggcca tgacgaaaga caacaatctg ttggggcgct 1860
tcgagctgag cggcatccct ccggcccccga ggggcgtgcc ccagatcgag gtgaccttcg 1920
acatcgatgc caacggcatc ctgaacgtca cggccacgga caagagcacc ggcaaggcca 1980
acaagatcac catcaccaac gacaagggcc gcctgagcaa ggaggagatc gagecgcatgg 2040
tgcaggagggc ggagaagtac aaagcggagg acgaggtgca ggcgcgagagg gtgtcagcca 2100
agaacgccct ggagtcctac gccttcaaca tgaagagcgc cgtggaggat gaggggctca 2160
agggcaagat cagcgaggcc gacaagaaga aggttctgga caagtgtcaa gaggtcatct 2220
cgtggctgga cgccaacacc ttggccgaga aggacgagtt tgagcacaag aggaaggagc 2280
tgagcgaggt gtgtaacccc atcatcagcg gactgtacca ggggtgccggt ggtcccgggc 2340
ctggcggtt cggggctcag ggtcccaagg gagggctctg gtcaggccct accattgagg 2400
aggtggattta ggggcctttg ttcttttagta tgtttgtctt tgaggtggac tgttgggact 2460
caaggacttt gctgctgttt tctatgtca tttctgcttc agctctttgc tgcttcactt 2520
ctttgtaaag ttgtaacctg atggtaatta gctggcttca ttatttttgt agtacaaccg 2580
atatgttcat tagaattctt tgcatttaat gttgatactg taagggtggt tcgttccctt 2640
taaataaata aacactgcca ccttctgtac gagtttgttt gttttttttt tttttttttt 2700
tttttgcttg gcgaaaacac tacaaaggct gggaatgtat gtttttataa tttgtttatt 2760
taaataatgaa aaataaaatg ttaaactttt tcttgtctgt taatatgtga agataatgga 2820
tatttgcgga gggatagtgt ctgaatacca tctatcttta tagtctgaaa agaaca 2876

<210> 6

<211> 6032

<212> DNA

<213> Homo sapiens

<400> 6

gaattccgtg ggcggaggtc tgggatctcc tggctgttgc tgtcttctgc tctcatcctg 60
caggtgggac tctcagctga caccatgagt agtgacactg aaatggaagt gttcggcata 120
gctgctcctt tctccggaa gtcagaaaag gagaggatcg aggctcagaa ccagcccttt 180
gatgccaaga cgtattgctt cgtgggtggac tcaaaggaag aatatgccaa ggggaaaatc 240
aagagttctc aggatgggaa ggtcactgtg gaaactgagg acaacaggac cctgggtggc 300
aaaccagagg atgtgtacgc catgaacccc cccaagtctg acaggatcga agacatggcc 360

atgctgacgc	acctgaatga	gccagccgtg	ctgtacaacc	tgaaggaccg	ttacacatct	420
tggatgatct	atacctactc	aggcctcttc	tgtgtcactg	tcaacccta	caagtggctg	480
ccggtgtaca	accccgaggt	ggtggaaggc	taccgaggca	aaaagcgcca	ggaggcccca	540
ccccacatct	tctccatctc	tgacaacgcc	tatcagttca	tgctgactga	tcgtgaaaac	600
cagtccattc	tgatcacggg	agaatccggg	gcaggaaaga	ctgtgaacac	caaacgggtc	660
atccagtact	ttgcaacaat	tgacagctact	ggggacctgg	ccaagaagaa	ggactccaaa	720
atgaagggga	ctctggaaga	tcaaatcatc	agtgccaatc	ccctgctgga	ggcctttggg	780
aacgccaaga	ctgtgaggaa	tgacaactcc	tcccgttttg	gcaagttcat	ccgaatccat	840
tttggaacca	ctgggaagct	ggcctctgca	gatattgaaa	cttatcttct	ggaaaaatca	900
agagtcactt	tccagctgaa	ggctgaaaga	agctaccaca	tcttctacca	gattctttct	960
aacaagaagc	ctgagctcat	agagctgctg	cttattacga	ccaaccctta	cgactacccg	1020
ttcattagcc	agggggagat	cctggtggcc	agcatagatg	atcgagagga	gctgctggct	1080
acagacagcg	ccattgacat	cctgggcttc	acccagaag	agaaatctgg	gctctacaag	1140
ctgacgggag	ccgtgatgca	ctacgggaac	atgaagttca	agcagaagca	gcgagaggag	1200
caggccgagc	cggatggcac	agaagtggct	gacaaaacag	cctatctgat	gggcctgaac	1260
tcttcggacc	tcctaaaagc	tttgtgcttt	cctagagtga	aagttgggaa	tgagtacgtt	1320
accaaaggte	aaactgtgga	tcaggttcac	catgctgtga	atgctctttc	aaaatcagtt	1380
tatgaaaagt	tgttcttgtg	gatggtcact	cgcattaacc	agcaactgga	tacgaagctt	1440
ccaagacaac	acttcattgg	tgttttggac	attgcaggct	ttgaaatctt	tgagtataac	1500
agcctggagc	agctgtgcat	caacttcacc	aatgagaaac	tgcaacagtt	tttcaaccac	1560
cacatgttcg	tgctggagca	ggaggagtag	aagaaggaag	gcatcgagtg	gacgttcatt	1620
gacttcggga	tggacctggc	tgccctgcac	gagctcatcg	agaagcctat	gggcatcttc	1680
tccatcctgg	aagaggagtg	catgttcccc	aaggcaacag	acacctcctt	caagaacaag	1740
ctgtatgacc	agcatcttgg	aaagtccaac	aacttcaga	agcccaaggt	ggtcaaaggc	1800
agggcagagg	ctcacttctc	actgatccac	tatgcgggca	ccgtggacta	cagtgtctca	1860
ggttggtctg	agaagaacaa	ggacctctg	aacgagactg	tggttgggct	gtaccagaag	1920
tcttccaaca	ggctcctggc	acacctctat	gccacgtttg	ccaoggcgga	tgctgacagt	1980
ggaaagaaga	aagttgcaa	gaagaagggt	tcttccttcc	aaactgtctc	tgcccttttc	2040
agggaaaacc	tgaacaagct	gatgtcaaat	ttaagaacta	ctcaccctca	ttttgtgcgt	2100

- 10 -

tgtataattc	ccaatgaaac	caaaactcca	ggggctatgg	aacacagcct	tgttctgcac	2160
cagctgcggt	gtaacggtgt	cctggagggc	atccgcctct	gcaggaaagg	gttcccaaac	2220
aggattctct	atggagattt	taaacaaaga	taccgagtgc	tgaatgccag	tgcaatcctg	2280
gagggacaat	tcattgacag	caagaaagcc	tgtgaaaagc	ttctggcatc	cattgatatt	2340
gaccacactc	agtacaaatt	tggacatacc	aaggtgttct	tcaaggctgg	cttgctggga	2400
accctggaag	agatgcggga	tgaccgcctg	gccaaactaa	tcacccggac	acaagctgtg	2460
tgacagaggt	tcctcatgcg	tgtggaattc	cagaagatgg	tgacagaggag	ggagtccatc	2520
ttctgcatcc	agtacaacat	tcgctcattc	atgaacgtca	agcactggcc	ctggatgaaa	2580
ctctttcttca	agatcaagcc	cctcctcaag	agtgcggaga	ctgagaaaga	gatggccacc	2640
atgaaggaag	aattccagaa	aaccaaagat	gaactcgcca	agtcggaggc	aaagaggaag	2700
gagctagagg	aaaaactggc	gactctgggc	caagagaaaa	atgacctgca	gctccaagta	2760
caagctgaaa	gcgaaaattt	gttggtatgct	gaggaaagat	gcgatcagct	gatcaaagcc	2820
aaattccagc	tcgaggccaa	gatcaaggag	gtgacagaga	gagctgaaga	tgaggaggag	2880
atcaatgctg	agctgacggc	caagaagagg	aaactggagg	atgaatgctc	agagctcaag	2940
aaagacattg	atgaccttga	gttgaccctg	gccaaagggt	agaaggagaa	gcatgccacg	3000
gagaacaagg	ttaaaaaact	tactgaggaa	ctctccgggt	tagatgaaac	aattgcaaag	3060
ttaaccagag	agaagaaggc	cctccaagag	gcgcaccagc	aggccttgga	tgacctccaa	3120
gctgaagaag	acaaagtcaa	ttctttgaac	aaaaccaaga	gcaaactgga	acagcaagtg	3180
gaagacctgg	aaagctccct	agaacaagaa	aagaagctcc	gcgtagacct	ggaaaggaac	3240
aaaaggaaat	tggaaggaga	cttgaagctt	gctcaagagt	ccatattaga	tctggagaat	3300
gacaagcaac	agctggacga	aaggctcaag	aagaaagatt	ttgaatattg	tcaacttcaa	3360
agcaaagtgg	aagatgagca	gacactgggc	ctccagtttc	agaagaaaat	caaagagttg	3420
caggctcgaa	ttgaggagct	ggaagaggag	atagaggcgg	agagggccac	ccgcgcgaag	3480
acagagaaac	agcgcagcga	ctatgcccg	gagctggagg	agctgagcga	gcggctggag	3540
gaggcgggag	gcgtcacctc	cacgcagata	gagctcaaca	agaagcggga	ggctgagttc	3600
ctgaagctgc	gcagggacct	ggaggaggcc	acactgcagc	acgaagccat	ggtggccacg	3660
ctgaggaaga	agcatgcgga	tagtgtggcc	gagcttgggg	agcagattga	caacctgcag	3720
cgggtcaage	agaagctgga	gaaggagaag	agcgagttca	agctggagat	cgatgacctc	3780
tcacgcagca	tggagagtgt	gtcgaaatct	aaggcaaate	tggaaaaaat	ctgccgaacc	3840
ctggaggatc	agttaagtga	ggccaggggc	aagaatgagg	aaattcagag	gagcctgagc	3900

- 11 -

gagctgacca	cacagaagtc	tcgtttgcag	accgaggetg	gtgagctgag	tcgtcagctg	3960	
gaagaaaaag	aaagcatagt	atcccaactt	tccaggagca	agcaagcctt	taccagcaa	4020	
acagaagagc	tcaagaggca	gctggaggaa	gagaacaagg	ccaagaacgc	cctggcgcac	4080	
gccctgcagt	cctcccgcca	cgactgtgac	ctgctgcggg	aacagtatga	ggaggagcag	4140	
gaaggcaaag	ctgagctgca	gagggcgctg	tccaaggcca	atagttaggt	tgcccagtgg	4200	
agaaccaa	at	acgagacgga	cgccatccag	cgcacagaag	agctggagga	ggcccaagaa	4260
aaacttgctc	agcgccttca	agattccgag	gaacagggtt	aggcagtga	tgctaaatgt	4320	
gcttcactgg	agaagaccaa	gcagaggctg	caaggagagg	tggaggatct	gatggttgat	4380	
gttgaaagag	ccaattcctt	ggccgcccgt	ctggacaaga	agcagaggaa	ctttgacaag	4440	
gtgttggcag	agtggaagac	aaagtgtgag	gagagccaag	cagagctgga	ggcatccctg	4500	
aaggagtccc	gctccttgag	cactgagctc	ttcaaactga	aaaatgccta	cgaggaagcc	4560	
ttagatcaac	ttgaaactgt	gaaacgggaa	aataagaact	tagagcagga	gatagcagat	4620	
ctcacagaac	aaattgctga	aaatggcaaa	accatccatg	aactggagaa	atcaagaaag	4680	
cagattgagc	tggaaaaggc	tgatatccag	ctggctctcg	aggaagcaga	ggctgctctt	4740	
gagcatgaag	aagccaagat	cctccgaatc	cagcttgaat	tgacacaagt	gaaatcagaa	4800	
attgatagaa	agattgccga	gaaggatgaa	gagatcgagc	agctgaagag	gaactaccag	4860	
agaacagtgg	aaaccatgca	gagcgccctg	gacgcccagg	tgccggagcag	gaatgaagcc	4920	
atccggctca	agaagaagat	ggaggggggac	ctgaatgaaa	tcgagatcca	gctgagccac	4980	
gccaaccgcc	aggcggcgga	gaccctcaaa	cacctcagga	gtgtccaggg	acagctgaag	5040	
gatacgagc	tccacctgga	tgatgccctc	cgaggccagg	aggacctgaa	ggagcagctg	5100	
gcgattgtgg	agcgcagagc	caacctgctg	caggccgagg	tggaggagct	gcgggctact	5160	
ctggagcaga	cggagagggc	ccggaaactg	gcggaacagg	agctcctgga	ctccaacgag	5220	
agggtgcagc	tgctgcatac	ccagaacacc	agcctcatcc	acaccaagaa	gaagctggag	5280	
acagacctca	tgagctcca	gagttaggta	gaagatgcca	gcagggatgc	aaggaacgct	5340	
gaggagaagg	ccaagaaggc	catcacggac	gctgccatga	tggcggagga	gctgaagaag	5400	
gagcaggaca	ccagcgccca	ccttgagcgg	atgaagaaga	acctggaaca	gacggtgaag	5460	
gacctgcagc	atcgtctaga	tgaggccgag	cagctggcgc	tgaagggcgg	gaagaagcag	5520	
atccagaaac	tggagaccag	gatccgagag	ctggagtttg	aacttgaggg	agagcagaag	5580	
aagaacacag	agtctgttaa	gggcctgagg	aagtatgagc	ggaggggtcaa	ggagctgacg	5640	

- 12 -

taccagagtg aagaggacag gaagaatgtg ctgagattgc aggatctggt ggataaactg 5700
 caagtgaag tcaagtccta caagaggcag gcggaggagg ctgatgaaca agccaatgct 5760
 catctcacca aattccggaa agctcagcat gagctggagg aggccgagga acgtgcggat 5820
 atcgcagaat ctcaagtcaa caagctccgc gctaagactc gagacttcac ctccagcagg 5880
 atggtggtcc acgagagtga agagtgagcc agcccttctg gagcaggagc aggacagaag 5940
 atatgcaaaa tgtatatattt cttgattcct gaccattgat acttaatgtc catgtgactc 6000
 tttttcacat gcaataaact ttgctttgtt tc 6032

<210> 7

<211> 3060

<212> DNA

<213> Homo sapiens

<400> 7

gggcaggctc agtgtgagtg aactggaggc ttctctacaa catgacccaa aggagcattg 60
 caggtcctat ttgcaacctg aagtttgtga ctctcctggt tgccttaagt tcagaactcc 120
 cattcctggg agctggagta cagcttcaag acaatgggta taatggattg ctcatcgcca 180
 ttaatcctca ggtacctgag aatcagaacc tcctctcaaa cattaaggaa atgataactg 240
 aagcttcatt ttacctatatt aatgctacca agagaagagt atttttcaga aatataaaga 300
 ttttaatacc tgccacatgg aaagctaata ataacagcaa aataaaacaa gaatcatatg 360
 aaaaggcaaa tgtcatagtg actgactggg atgggggcaca tggagatgat ccatacaccc 420
 tacaatacag aggggtgtgga aaagaggga aatacattca tttcacacct aatttcctac 480
 tgaatgataa cttaacagct ggctacggat cagcaggccg agtggtttgtc catgaatggg 540
 cccacctccg ttgggggtgtg ttogatgagt atatcaatga caaacctttc tacataaatg 600
 ggcaaaatca aattaaagtg acaagggtgtt catctgacat cacaggcatt tttgtgtgtg 660
 aaaaagggtcc ttgcccccaa gaaaactgta ttattagtaa gcttttttaa gaaggatgca 720
 cctttatcta caatagcacc caaaatgcaa ctgcatcaat aatgttcatt caaagtttat 780
 cttctgtggt tgaattttgt aatgcaagta ccacacacca agaagcacca aacctacaga 840
 accagatgtg cagcctcaga agtgcattgg atgtaatcac agactctgct gactttcacc 900
 acagctttcc catgaatggg actgagcttc cacctcctcc cacattctcg cttgtacagg 960
 ctggcgacaa agtggtctgt ttagtgctgg atgtgtccag caagatggca gaggctgaca 1020

- 13 -

gactccttca actacaacaa gccgcagaat tttatttgat gcagattggt gaaattcata	1080
ccttcgtggg cattgccagt ttcgacagca aaggagagat cagagccag ctacaccaa	1140
ttaacagcaa tgatgatcga aagttgctgg tttcatatct gccaccact gtatcagcta	1200
aaacagacat cagcatttgt tcagggctta agaaaggatt tgaggtggtt gaaaaactga	1260
atggaaaagc ttatggctct gtgatgatat tagtgaccag cggagatgat aagcttcttg	1320
gcaattgctt acccactgtg ctcagcagtg gttcaacaat tcactccatt gccctgggtt	1380
catctgcagc cccaaatctg gaggaattat cacgtcttac aggaggttta aagttctttg	1440
ttccagatat atcaaactcc aatagcatga ttgatgcttt cagtagaatt tcctctggaa	1500
ctggagacat tttccagcaa catattcagc ttgaaagtac aggtgaaaat gtcaaacctc	1560
accatcaatt gaaaaacaca gtgactgtgg ataatactgt gggcaacgac actatgtttc	1620
tagttacgtg gcaggccagt ggtcctcctg agattatatt atttgatcct gatggacgaa	1680
aatactacac aaataatttt atcaccaatc taacttttcg gacagctagt ctttggaattc	1740
caggaacagc taagcctggg cactggactt acaccctgaa caatacccat cattctctgc	1800
aagccctgaa agtgacagtg acctctcgcg cctccaactc agctgtgccc ccagccactg	1860
tggaagcctt tgtggaaaga gacagcctcc attttcctca tcctgtgatg atttatgcca	1920
atgtgaaaca gggattttat ccattctta atgccactgt cactgccaca gttgagccag	1980
agactggaga tcctgttacg ctgagactcc ttgatgatgg agcaggtgct gatgttataa	2040
aaaatgatgg aatttactcg aggtattttt tctcctttgc tgcaaattggt agatatagct	2100
tgaaagtgca tgtcaatcac tctcccagca taagcacccc agcccactct attccaggga	2160
gtcatgctat gtatgtacca ggttacacag caaacggtaa tattcagatg aatgctccaa	2220
ggaaatcagt aggcagaaat gaggaggagc gaaagtgggg ctttagccga gtcagctcag	2280
gaggctcctt ttcagtgtg ggagttccag ctggccccca ccctgatgtg tttccaccat	2340
gcaaaattat tgacctggaa gctgtaaaag tagaagagga attgacccta tcttggaacg	2400
cacctggaga agactttgat cagggccagg ctacaagcta tgaaataaga atgagtaaaa	2460
gtctacagaa tatccaagat gactttaaca atgctatttt agtaaataca tcaaagcgaa	2520
atcctcagca agctggcatc agggagatat ttacgttctc accccaaatt tccacgaatg	2580
gacctgaaca tcagccaaat ggagaaacac atgaaagcca cagaatttat gttgcaatac	2640
gagcaatgga taggaactcc ttacagtctg ctgtatctaa cattgccag gcgcctctgt	2700
ttattcccc caattctgat cctgtacctg ccagagatta tcttatattg aaaggagttt	2760

- 14 -

taacagcaat gggtttgata ggaatcattt gccttattat agttgtgaca catcatactt	2820
taagcaggaa aaagagagca gacaagaaag agaattggaac aaaattatta taaataaata	2880
tccaaagtgt cttccttctt agatataaga cccatggcct tcgactacaa aaacatacta	2940
acaaagtcaa attaacatca aaactgtatt aaaatgcatt gagtttttgt acaatacaga	3000
taagatTTTT acatggtaga tcaacaattc tttttggggg tagattagaa aacccttaca	3060

<210> 8

<211> 2878

<212> DNA

<213> Homo sapiens

<400> 8

cccgatgagc agcgaacagg gaatgacagt tccaccagaa gacgattaag ccacagcctc	60
taattggaac ggcatttgta cagtcagaga ctcttaccag acatctccag gaatctgtga	120
gccattgtca aaacgtccat tttcatctgg ctgtgaaagt gaggaccaca acaggtaggt	180
attggtagaa acaggagtcc tcagagaagc cccaagatgc agcctgaggg agcagaaaag	240
ggaaaaagct tcaagcagag actggtcttg aagagcagct tagcgaaaga aaccctctct	300
gagttcttgg gcacgttcat cttgattgtc cttggatgtg gctgtgttgc ccaagctatt	360
ctcagtcgag gacgttttgg aggggtcatc actatcaatg ttggattttc aatggcagtt	420
gcaatggcca tttatgtggc tggcgggtgc tctggtggtc acatcaacc cagctgtgtct	480
ttagcaatgt gtctcttttg acggatgaaa tggttcaa at tgccatttta tgtgggagcc	540
cagttcttgg gagcctttgt gggggctgca accgtctttg gcatttacta tgatggactt	600
atgtcctttg ctggtggaaa actgctgac gtgggagaaa atgcaacagc acacattttt	660
gcaacatacc cagctccgta tctatctctg gcgaacgcat ttgcagatca agtgggtggc	720
accatgatac tcttcataat cgtctttgcc atttttgact ccagaaactt gggagcccc	780
agaggcctag agcccattgc catcggcctc ctgattattg tcattgcttc ctccctggga	840
ctgaacagtg gctgtgccat gaaccagct cgagacctga gtcccagact tttcactgcc	900
ttggcaggct gggggtttga agtcttcaga gctggaaaca acttctggtg gattcctgta	960
gtgggccctt tggttggtgc tgtcattgga ggctcatct atgttcttgt cattgaaatc	1020
caccatccag agcctgactc agtctttaag gcagaacaat ctgaggacaa accagagaaa	1080
tatgaactca gtgtcatcat gtagtggcat gctcagctct ggatttgcag tcagtttggg	1140

- 15 -

attctcttca gaaagatggc atctaagtgt ctgtgttctt gtaagcctga ggtggaatcc 1200
 acccagtttt gtctgctagc catatgggac atctaattgg aaaagcatct gcataaaagt 1260
 ttggaacaa tgaccacttc tctaccattg tccccaccc ccacccccca gaataacgct 1320
 gactgtcccc tgaaacagcc ttctctcctg cctgttttat ttcatectcg atgggaattc 1380
 ttgctaggta agcactaata actcggcatc ttgacgatag tccattttgg gtggtttcag 1440
 ctgcactatc tgtatgaaat ggtgtcacca aaaccctttt cttcagtatc gacaaagatt 1500
 acattctgag taccaaccaa accctaaatt gaaagacaaa actatgggtt cagtcaacat 1560
 attcatgaat tagggagcta atgggttaag cttccagttc ccgctatgct actggatttg 1620
 tataaatact gatattctcc aaacctagtg gtgtaggag caagagaatg cagctggaag 1680
 gcacaagggg aggacattgt ggcattcaga aactgcagga gacaagatga atttgagaag 1740
 ccaaattgaa tttttaatgg aaaccattta tcagattaat ctcttgctct cctgcatttt 1800
 agaggacacc aattaatttc ctggtcttta gtatataata acctaaaata ccattgtaac 1860
 ctcagtcatg aaaaatacat cactctgtct ttttagctca aatgtatttt cctaattgcc 1920
 cacttgagaa cagacatttg acaagttata tcaacgactg tgcttgcca ttattttaca 1980
 catgccctag aagccaaaac tgaaagccac tggatcctgg tctagctgaa tcttcagagt 2040
 gggaggtctc caaaaagata ttaccttatt gggcttaaca attcacaagg cactttcaca 2100
 cccattatct aatttaatcc tcataatgac tatgtgaggc aaatgccaca ttgcccattt 2160
 ttcagataaa gaaacaaaat cttagggaag ataagttgag ttgtccaaga gcacactgaa 2220
 agttgaatgt tatctaattgc attcctctac ctttcagaag atcagtagct ggctgagaat 2280
 ctttgccaaa tcttccttgc tagccagaag tggaattggc agcttctaga atatgtacac 2340
 ctctggacaa aatgttcttc aatcttaaga tacaaagacc ctcatgtctt gggctctattc 2400
 ccacacttac tgagtacaga tgaaggaaag tggtagcaat ttaatcataa ctttcatttg 2460
 ctgaaaaaca ttatgagaag gcctcccttc ctaagccacc tctggtcttg ctaagtcttg 2520
 atcttgcttc ctgccagcac caaacattac attcagggga tttcctctgg ctcagtcttt 2580
 tcccttgaa gttctctaata agatgttact tttgacaaaa gatcgccctat gagttacaag 2640
 caccagggga tgctctacat caagggatgc accttcagtc aaactgtcaa aaagcccaga 2700
 attcccaaag gcattagggt tcccaactgc tttgtgctga tatcagaaca gcagaaatta 2760
 aatgtgaaat gtttctgatg acttatgttc tacaatctat ggacatacgg gatttttttt 2820
 tcttgctttg aagctacctg gatatttcct atttgaaata aaattgttcg gtcattgg 2878

- 16 -

<210> 9
<211> 1442
<212> DNA
<213> Homo sapiens

<400> 9
ccgggggatcc acgcgcgcgc ccacccctgc ccgcccgcaca gcgcgcgcgc ctgccccgcc 60
atgggtcgac agaaggagct ggtgtcccgc tgcggggaga tgctccacat ccgctaccgg 120
ttgctccgac aggcgcctggc cgagtgcctg gggaccctca tccctcgtgat gtttggtgtg 180
ggctocgtgg cccagggttg gctcagccgg ggcacccacg gtggtttccct caccatcaac 240
ctggcctttg gctttgctgt cactctgggc atcctcatcg ctggccaggt ctctggggcc 300
cacctgaacc ctgccgtgac ctttgccatg tgcttcctgg ctctgtgagcc ctggatcaag 360
ctgcccacat acaccctggc acagacgctg ggagccttct tgggtgctgg aatagttttt 420
gggctgtatt atgatgcaat ctggcacttt gccgacaacc agctttttgt ttcgggcccc 480
aatggcacag ccggcatctt tgctacctac ccctctggac acttgatat gatcaatggc 540
ttctttgacc agttcatagg cacagcctcc cttatcgtgt gtgtgctggc cattgttgac 600
ccttacaaca accccgtccc ccgaggcctg gaggccttca ccgtgggcct ggtggtcctg 660
gtcattggca cctccatggg cttcaactcc ggctatgccg tcaaccctgc ccgggacttt 720
ggcccccgcc tttttacagc ccttgccggc tggggctctg cagtcttcac gaccggccag 780
cattggtggt ggggtgcccac cgtgtcccca ctccctgggt ccattgcggg tgtcttcgtg 840
taccagctga tgatcggctg ccacctggag cagccccac cctccaacga ggaagagaat 900
gtgaagctgg cccatgtgaa gcacaaggag cagatctgag tggcaagggc catctcccac 960
tccgctgccc tggccttgag catccactga ctgtccaagg ccactcccaa gaagcccccc 1020
ttcacgatcc accctttcag gctaaggagc tccctatcta cctcaccac acgaagacag 1080
ccccttcagg atttccactg gaccttgccc aaatagcacc ttaggccact gccctaagc 1140
tggggtggaa ccggaatttg ggtcaataca tccttttgtc tccaagggga agagaatggg 1200
cagcaggtat gtgtgtgtgt gtgcatgtgt gcatgtgtgt gcatgtgtgt gcaggggtgt 1260

- 17 -

gtgtgtgggg ggggttccca gatattcagg gcaagaccag tcggaaggat ctgctattgg 1320
ggacccagag acagggaggc agcctgtcca tctgtgcata aggagaggaa agttccaggg 1380
tgtgtatgtt ttcagggggc ttcacatgga ggagctgcag atagatatgt gtttctccgg 1440
aa 1442

<210> 10

<211> 1806

<212> DNA

<213> Homo sapiens

<400> 10

gccgctcgct cggtccgct ccctggctcg gctccctgcc tccgcgtcgc agcccccgcc 60
gtageccgct ccgagcccgcc cgccacatcc tctgagaaga tggctgtgcc acccacgtat 120
gccgatcttg gcaaattctgc cagggatgtc ttcaccaagg gctatggatt tggcttaata 180
aagcttgatt tgaaaacaaa atctgagaat ggattggaat ttacaagctc aggtcagcc 240
aacactgaga ccaccaaagt gacgggcagt ctggaaacca agtacagatg gactgagtac 300
ggcctgacgt ttacagagaa atggaatacc gacaatacac taggcaccga gattactgtg 360
gaagatcagc ttgcacgtgg actgaagctg accttcgatt catccttctc acctaacact 420
gggaaaaaaaa atgctaaaat caagacaggg tacaagcggg agcacattaa cctgggctgc 480
gacatggatt tcgacattgc tgggccttcc atccggggtg ctctggtgct aggttacgag 540
ggctggctgg ccggctacca gatgaatttt gagactgcaa aatcccgagt gaccagagc 600
aactttgcag ttggctacaa gactgatgaa ttccagcttc acactaatgt gaatgacggg 660
acagagtttg gcggctccat ttaccagaaa gtgaacaaga agttggagac cgctgtcaat 720
cttgectgga cagcaggaaa cagtaacacg cgcttcggaa tagcagccaa gtatcagatt 780
gaccctgacg cctgcttctc ggctaaagtg aacaactcca gcctgatagg tttaggatac 840
actcagactc taaagccagg tattaaactg aactgtcag ctcttctgga tggcaagaac 900
gtcaatgctg gtggccacaa gcttggtcta ggactggaat ttcaagcata aatgaatact 960
gtacaattgt ttaattttta actattttgc agcatagcta ccttcagaat ttagtgtatc 1020
ttttaatgtt gtatgtctgg gatgcaagta ttgctaaata tgtagccct ccaggttaaa 1080
gttgattcag ctttaagatg ttacccttcc agaggtagag aagaaacctt tttccaaaaa 1140
aggtcccttc agtggttagac tcggggagaa cttggtggcc cctttgagat gccaggtttc 1200

- 18 -

ttttttatct agaaatggct gcaagtggaa gcggataata tgtaggcact ttgtaaattc	1260
atattgagta aatgaatgaa attgtgattt cctgagaatc gaaccttggt tccctaaccc	1320
taattgatga gaggctcgct gcttgatggg gtgtacaaac tcacctgaat gggacttttt	1380
tagacagatc ttcatgacct gttcccaccc cagttcatca tcatctcttt tacaccaaaa	1440
ggctctgcagg gtgtggtaac tgtttctttt gtgccatttt ggggtggaga aggtggatgt	1500
gatgaagcca ataattcagg acttattcct tcttggtgtg tgtttttttt tggcccttgc	1560
accagagtat gaaatagctt ccaggagctc cagctataag cttggaagtg tctgtgtgat	1620
tgtaatcaca tggtgacaac actcagaatc taaattggac ttctgttgta ttctcaccac	1680
tcaatttggt ttttagcagt ttaatgggta catttttagag tcttccattt tgttggaatt	1740
agatcctccc cttcaaatgc tgtaattaac aacacttaaa aaacttgaat aaaatattga	1800
aacctc	1806

<210> 11

<211> 800

<212> DNA

<213> Homo sapiens

<400> 11

gaattccggg caaagctctt tcaccagatg tagactgtag ccctgctgcc ttcctccag	60
cgagtctgcc agcatgcttc ttcctccttt ttatatgttc tttgcttctt tccctccctc	120
cttgctctct gtcgccgtct cttctggcgc cgctgctccc ggaggagctc ccggcacggc	180
gatgggttct cgggcctcca cgttactgcg ggacgaagag ctcgaggaga tcaagaagga	240
gaccggcttt tcccacagtc aaatcactcg cctctacagc cggttcacca gcctggacaa	300
aggagagaat gggactctca gccgggaaga tttccagagg attccagaac ttgccatcaa	360
cccactgggg gaccggatca tcaatgcctt ctttccagag ggagaggacc aggtaaactt	420
ccgtggattc atgcgaactt tggctcattt ccgccccatt gaggataatg aaaagagcaa	480
agatgtgaat ggacccgaac cactcaacag ccgaagcaac aaactgcact ttgcttttcg	540
actatatgat ttggataaag atgaaaagat ctcccgtgat gagctgttac aggtgctacg	600
catgatggtc ggagtaaata tctcagatga gcagctgggc agcatcgcag acaggaccat	660
tcaggaggct gatcaggatg gggacagtgc catatctttc acagaatttg ttaaggtttt	720

- 19 -

ggagaaggtg gatgtagaac agaaaatgag catccgattt cttcactaaa ggagaccaaa 780
ctgttcttgc ggtctagtat 800

<210> 12

<211> 1935

<212> DNA

<213> Homo sapiens

<400> 12

ctggtcccga gcacgagctg tgaggggatt cacttgtgtg cggaactcct cggaaccatg 60
gcgtcccttt cccttgcacc tgttaacatc tttaaggcag gagctgatga agagagagca 120
gagacagctc gtctgacttc ttttattggt gccatcgcca ttggagactt ggtaaagagc 180
accttgggac ccaaaggcat ggacaaaatt cttctaagca gtggaogaga tgctctctt 240
atggtaacca atgatggtgc cactattcta aaaaacattg gtgttgacaa tccagcagct 300
aaagttttag ttgatatgtc aagggttcaa gatgatgaag ttggtgatgg cactacctct 360
gttaccgttt tagcagcaga attattaagg gaagcagaat ctttaattgc aaaaaagatt 420
catccacaga ccatcatagc gggttggaga gaagccacga aggctgcaag agaggcgctg 480
ttgagttctg cagttgatca tggttccgat gaagttaaatt tccgtcaaga tttaatgaat 540
attgcgggca caacattatc ctcaaaaactt cttactcatc acaaagacca ctttacaag 600
ttagctgtag aagcagttct cagactgaaa ggctctggca acctggaggc aattcatatt 660
atcaagaagc taggaggaag tttggcagat tcctatttag atgaaggctt cctgttggat 720
aaaaaaattg gagtaaatca accaaaacga attgaaaatg ctaaaattct tattgcaaatt 780
actggtatgg atacagacaa aataaagata tttggttccc gggtaagagt tgactctaca 840
gcaaagggtg cagaaataga acatgcggaa aaggaaaaaa tgaaggagaa agttgaacgt 900
attcttaagc atggaataaa ttgctttatt aacaggcaat taatttataa ttatcctgaa 960
cagctctttg gtgctgctgg tgtcatggct attgagcatg cagattttgc aggtgtggaa 1020
cgctagctc ttgtcacagg tggtgaaatt gcctctacct ttgatcacc agaactggtg 1080
aagcttgga gttgcaaact tatcgaggaa gtcattgatt gagaagacaa actcattcac 1140
ttttctgggg ttgcccttgg tgaggcttgt accattgttt tgcgtgggtgc cactcaacaa 1200
attttagatg aagcagaaag atcattgcat gatgctcttt gtgttcttgc gcaaactgta 1260
aaggactcta gaacagttta tggaggagge tgttctgaga tgttgatggc tcatgctgtg 1320

- 20 -

acacagcttg ccaatagaac accaggcaaa gaagctgttg caatggagtc ttatgctaaa 1380
 gcactgagaa tggtgccaac catcatagct gacaatgcag gctatgacag tgcagacctg 1440
 gtggcacage tcagggetgc tcacagtga ggaatacca ctgctggatt ggatatgagg 1500
 gaaggcacca ttggagatat ggctatcctg ggtataacag aaagttttca agtgaagcga 1560
 caggttcttc tgagtgcagc tgaagcagca gaggtgattc tgcgtgtgga caacatcatc 1620
 aaagcggcac ccaggaaacg tgtccctgat caccaccctt gttaagcatt cccacgtgct 1680
 gtcgatcttt ggaccagttt ctagcaaagt tgtgtttgaa agatactcta ttaaagaaga 1740
 ctgtggaatc tgtttatcgg tgcccattat atccttaagt ttggatattt agctgacctt 1800
 cgctttaaca taggtctaata ttatttgccg tgctattttc catacaaatc agttgattta 1860
 aaggagttca tttcgcatat tgggcattaa aataaaaatt tgaacaatga aaggaaaaaa 1920
 aggagaaaaa aaaaa 1935

<210> 13

<211> 1528

<212> DNA

<213> Homo sapiens

<400> 13

cagtgccttg gtaatgacca gggctccaga aagagatgtc cttgtggctg ggggcccctg 60
 tgcctgacat tcctcctgac tctgcggtgg agctgtggaa gccaggcgca caggatgcaa 120
 gcagccaggc ccagggaggc agcagctgca tcctcagaga ggaagccagg atgccccact 180
 ctgctggggg tactgcaggg gtggggctgg aggtgcaga gcccacagcc ctgctcacca 240
 gggcagagcc cccttcagaa cccacagaga tccgtccaca aaagcggaaa aaggggccag 300
 cccccaaaat gctggggaac gagctatgca gcgtgtgtgg ggacaaggcc tcgggcttcc 360
 actacaatgt tctgagctgc gagggctgca agggattctt ccgccgcagc gtcataagg 420
 gagcgacta catctgccac agtggcggcc actgccccat ggacacctac atgcgtcgca 480
 agtgccagga gtgtcggtt cgcaaatgcc gtcaggctgg catgcgggag gagtgtgtcc 540
 tgtcagaaga acagatccgc ctgaagaaac tgaagcggca agaggaggaa caggctcatg 600
 ccacatcctt gccccccagg cgttcctcac cccccaaaat cctgccccag ctcagcccgg 660
 aacaactggg catgatcgag aagctcgtcg ctgccagca acagtgtaac cggcgctcct 720

- 21 -

tttctgaccg gcttcgagtc acgccttggc ccatggcacc agatccccat agccgggagg	780
cccgtcagca gcgctttgcc cacttcactg agctggccat cgtctctgtg caggagatag	840
ttgactttgc taaacagcta cccggcttcc tgcagctcag ccgggaggac cagattgccc	900
tgctgaagac ctctgcgata gaggtgatgc ttctggagac atctcggagg tacaaccctg	960
ggagtgaagag tatcaccttc ctcaaggatt tcagttataa ccgggaagac tttgccaaag	1020
cagggtgca agtggaattc atcaacccca tcttcgagtt ctccagggcc atgaatgagc	1080
tgcaactcaa tgatgccgag tttgccttgc tcattgctat cagcatcttc tctgcagacc	1140
ggcccaacgt gcaggaccag ctccagggtg agaggctgca gcacacatat gtggaagccc	1200
tgcatgccta cgtctccatc caccatcccc atgaccgact gatgttccca cggatgctaa	1260
tgaaactggt gagcctccgg accctgagca gcgtccactc agagcaagtg tttgcactgc	1320
gtctgcagga caaaaagctc ccaccgctgc tctctgagat ctgggatgtg cacgaatgac	1380
tgttctgtcc ccatattttc tgttttcttg gccggatggc tgaggcctgg tggctgcctc	1440
ctagaagtgg aacagactga gaagggcaaa cattcctggg agctgggcaa ggagatcctc	1500
ccgtggcatt aaaagagagt caaagggt	1528

<210> 14

<211> 3678

<212> DNA

<213> Homo sapiens

<400> 14

gtgaagacat cgcgggggacc gattcaccat ggagggcgcc ggcggcgcca acgacaagaa	60
aaagataagt tctgaacgtc gaaaagaaaa gtctcgagat gcagccagat ctccggcgaag	120
taaagaatct gaagtttttt atgagcttgc tcatcagttg ccacttcacac ataatgtgag	180
ttcgcacatt gataaggcct ctgtgatgag gcttaccatc agctattttgc gtgtgaggaa	240
acttctggat gctggtgatt tggatattga agatgacatg aaagcacaga tgaattgctt	300
ttatttgaaa gccttggatg gttttgttat gggtctcaca gatgatgggtg acatgattta	360
catttctgat aatgtgaaca aatacatggg attaactcag tttgaactaa ctggacacag	420
tgtgtttgat ttactcatc catgtgacca tgaggaaatg agagaaatgc ttacacacag	480
aaatggcctt gtgaaaaagg gtaaagaaca aaacacacag cgaagctttt ttctcagaat	540
gaagtgtacc ctaactagcc gaggaagaac tatgaacata aagtctgcaa catggaaggt	600

- 22 -

attgcactgc acaggccaca ttcacgtata tgataccaac agtaaccaac ctcagtgtgg	660
gtataagaaa ccacctatga cctgcttggt gctgatttgt gaacccattc ctcacccatc	720
aaatattgaa attccttttag atagcaagac tttcctcagt cgacacagcc tggatatgaa	780
attttcttat tgtgatgaaa gaattaccga attgatggga tatgagccag aagaactttt	840
aggccgctca atttatgaat attatcatgc tttggactct gatcatctga ccaaaactca	900
tcatgatatg tttactaaag gacaagtcac cacaggacag tacaggatgc ttgccaaaag	960
aggtggatat gtctgggttg aaactcaagc aactgtcata tataacacca agaattctca	1020
accacagtgc attgtatgtg tgaattacgt tgtgagtggg attattcagc acgacttgat	1080
tttctccctt caacaaacag aatgtgtcct taaaccgggt gaatcttcag atatgaaaat	1140
gactcagcta ttcaccaaag ttgaatcaga agatacaagt agcctctttg acaaacttaa	1200
gaaggaacct gatgctttaa ctttgctggc ccagccgct ggagacacaa tcatatcttt	1260
agattttggc agcaacgaca cagaaactga tgaccagcaa cttgaggaag taccattata	1320
taatgatgta atgctcccct cacccaacga aaaattacag aatataaatt tggcaatgtc	1380
tccattacce accgctgaaa cgccaaagcc acttcgaagt agtgctgacc ctgcactcaa	1440
tcaagaagtt gcattaaaat tagaaccaaa tccagagtca ctggaacttt cttttaccat	1500
gccccagatt caggatcaga cacctagtcc ttccgatgga agcactagac aaagttcacc	1560
tgagcctaata agtccocagt aatattgttt ttatgtggat agtgatatgg tcaatgaatt	1620
caagttggaa ttggtagaaa aactttttgc tgaagacaca gaagcaaaga acccattttc	1680
tactcaggac acagatttag acttgagat gttagctccc tatatcccaa tggatgatga	1740
cttccagtta cgttccttcg atcagttgtc accattagaa agcagttccg caagccctga	1800
aagcgcaagt cctcaaagca cagttacagt attccagcag actcaaatac aagaacctac	1860
tgctaatagcc accactacca ctgccaccac tgatgaatta aaaacagtga caaaagaccg	1920
tatggaagac attaaaatat tgattgcac tccatctcct acccacatac ataaagaaac	1980
tactagtgcc acatcatcac catatagaga tactcaaagt cggacagcct caccaaacag	2040
agcaggaaaa ggagtcatag aacagacaga aaaatctcat ccaagaagcc ctaacgtgtt	2100
atctgtcgct ttgagtcaaa gaactacagt tcctgaggaa gaactaaatc caaagatact	2160
agctttgcag aatgctcaga gaaagcgaaa aatggaacat gatggttcac tttttcaagc	2220
agtaggaatt ggaacattat tacagcagcc agacgatcat gcagctacta catcactttc	2280
ttggaaacgt gtaaaaggat gcaaactctag tgaacagaat ggaatggagc aaaagacaat	2340

- 23 -

tattttaata ccctctgatt tagcatgtag actgctgggg caatcaatgg atgaaagtgg	2400
attaccacag ctgaccagtt atgattgtga agttaatgct cctatacaag gcagcagaaa	2460
cctactgcag ggtgaagaat tactcagagc tttggatcaa gttaactgag cttttttctta	2520
atttcattcc ttttttttga cactgggtggc tcactaccta aagcagtcta tttatatattt	2580
ctacatctaa ttttagaagc ctggctacaa tactgcacaa acttggttag ttcaattttt	2640
gatccccctt ctacttaatt tacattaatg ctcttttttta gtatgttctt taatgctgga	2700
tcacagacag ctcatTTTTct cagtttttttg gtattttaaac cattgcattg cagtagcatc	2760
attttaaaaa atgcaccttt ttattttattt atttttggct agggagttaa tccctttttc	2820
gaattatttt taagaagatg ccaatataat ttttgtaaga aggcagtaac ctttcatcat	2880
gatcataggc agttgaaaaa tttttacacc ttttttttca cattttacat aaataataat	2940
gctttgccag cagtacgtgg tagccacaat tgcacaatat attttcttaa aaaataccag	3000
cagttactca tggaatatat tctgcgttta taaaactagt ttttaagaag aaattttttt	3060
tggcctatga aattgttaaa cctggaacat gacattgtta atcatataat aatgattctt	3120
aaatgctgta tggtttatta tttaaattggg taaagccatt tacataatat agaaagatat	3180
gcatatatct agaaggtatg tggcatttat ttggataaaa ttctcaattc agagaaatca	3240
tctgatgttt ctatagtcac tttgccagct caaaagaaaa caatacccta tgtagttgtg	3300
gaagtttatg ctaatattgt gtaactgata ttaaacctaa atgttctgcc taccctgttg	3360
gtataaagat attttgagca gactgtaaac aagaaaaaaa aaatcatgca ttcttagcaa	3420
aattgcctag tatgttaatt tgctcaaaat acaatgtttg attttatgca ctttgctgct	3480
attaacatcc tttttttcat gtagatttca ataattgagt aattttagaa gcattatttt	3540
aggaatatat agttgtcaca gtaaataatct tgttttttct atgtacattg tacaattttt	3600
tcattccttt tgctctttgt ggttggtatc aacactaact gtattgtttt gttacatcaa	3660
ataaacatct tctgtgga	3678

- 24 -

<210> 15

<211> 5767

<212> DNA

<213> Homo sapiens

<400> 15

```

gagggaggag agttcacttt tacttcagtg tcagcgcgcg gcggccgtgg ctggctctgg      60
cgagagagca ccgagggagt gggtcgcaga tcttcgggcg gctaggggaa atcggcgaga      120
ggcgggatcc gagcgcgccg gcggggcgca gagcccgca gcctggccag cgagggtagc      180
cgcgggggggc gcgccccggg cgggcccccg gagacgcgca ggatgccaca cgaagagctg      240
ccgtcgctgc agagaccccg ctatggctct attgtggacg atgaaaggct ctctgcagag      300
gagatggatg agaggaggcg gcagaacatt gcttatgaat atctgtgcc a cttagaggaa      360
gccaaaaggt ggatggaagt ttgcttagtt gaagaattgc caccaaccac tgaattggaa      420
gaagggtccc ggaatggagt ttaccttgca aagttagcca agttctttgc cccgaaaatg      480
gtatcagaga aaaagatcta tgatgtggaa caaacacgtt ataagaagtc tggccttcat      540
tttcgacaca cagataatac cgtccagtgg ttaagagcga tggagtctat tggcttacct      600
aagatatttt atccagaaac aacagatgtc tatgatcgga aaaacatacc aagaatgata      660
tattgcattc acgcactgag tttgtatctg ttcaaactag gaatagcacc ccagatccag      720
gatttggttg gcaaagtaga cttcacagag gaggaatca gtaatatgag aaaagaactt      780
gagaaatatg gaatacagat gccatcttcc agcaaaatag gtggtattct ggccaatgaa      840
ctgtccgtgg atgaagctgc attacatgct gcagttatag ccattaatga agcagttgaa      900
aaaggaatag cagagcaaac cgttgtaaca ctaagaaacc caaatgcggt tttaacttta      960
gtggatgaca accttgcacc agaatatcag aaagaactct gggatgccaa aaagaaaaaa     1020
gaggaaaatg caagactgaa gaatagctgt atttcagaag aagaaagaga tgcttatgaa     1080
gaactgctga cacaagcaga aatccaaggc aatattaata aagtcaacag gcaggctgca     1140
gtggaccata tcaatgctgt cattccggaa ggtgaccccg agaatacgct gcttgcactg     1200
aagaaaccag aggccagct gcctgctgtt tatecctttg ctgctgccat gtatcagaac     1260
gaacttttca acctccagaa acagaacacc atgaactact tggcccacga ggagcttttg     1320
attgctgtgg aatgttgct tgctgttgct ttactaaacc aggccttgga aagcaacgat     1380
cttgtgtctg tgcagaatca actcagaagc cccgcaatag gcttaaacaa tctggacaag     1440

```

- 25 -

gcatatgtgg aacgttatgc aaacacacta ctctctgtta aactagaagt tttatcccaa	1500
gggcaagata acttaagctg gaatgaaatt cagaattgta ttgatatggg taatgctcaa	1560
attcaagaag aaaatgaccg agttgtagct gtaggggtaca tcaatgaagc tattgatgaa	1620
gggaatcctt tgaggacttt agaaactttg ctctaccta ctgcgaatat tagtgatgtg	1680
gaccagccc atgcccagca ctaccaggat gttttatacc atgctaaatc acagaaactc	1740
ggagactctg agagtgtttc caaagtgtt tggctggatg agatacagca agccgtcgat	1800
gaggccaacg tggacgagga cagagcaaaa caatgggtta ctctgggtgg tgatgttaat	1860
cagtgtttgg aaggaaaaaa atcaagtgat attttgtctg tattgaagtc ttccacttct	1920
aatgcaaag acataatccc ggagtgtgct gacaaatact atgatgccct tgtgaaggca	1980
aaagagctca aatctgaaag agtgtctagt gacggttcat ggctcaaact caacctgcac	2040
aaaaaatatg actactatta caacactgat tcaaaagaga gtccctgggt cacacctgaa	2100
tcatgcttct ataaagaatc atggctcaca ggaaaagaaa tcgaggacat tattgaggaa	2160
gtcacagtag gttacattcg tgagaatata tggctctgctt cagaagagtt gcttcttcgc	2220
tttcaagcca caagctcagg acccatcctt aggggaagagt ttgaagctag aaaatcattt	2280
ttgcatgaac aagaagagaa tgtgggtcaaa atacaggctt tttggaaagg atataaaca	2340
cgggaaggagt atatgcacag gcggcaaacg ttcattgata atactgattc tgttgtgaag	2400
attcagtcct gggtccgaat ggcaactgca agaaagagct atctttcaag actacagtat	2460
ttcagagatc ataataatga aattgtgaaa atacagtcac tgttgagagc gaacaaagct	2520
agagatgact acaaaacatt gggtggctct gaaaaccac cattaacagt aattcgcaaa	2580
tttgataacc tgctggacca aagtgatttg gatttccagg aggaactaga gggtgcacga	2640
ttaagggaag aagtagtgac caagatcagg gccaatcaac agctggaaaa agacctgaac	2700
ctgatggaca tcaagattgg actgctgggtg aagaacagga tcacactaga ggatgtaatt	2760
tcacacagta aaaagctgaa caagaaaaaa ggaggagaaa tggaaatact gaataacacc	2820
gacaaccaag gaataaaaag tttgagtaag gagaggagaa aaacactaga aacatatcag	2880
cagctgtttt accttttaca gaccaacct ttatacttgg ctaagctgat tttccagatg	2940
ccacagaaca agtccactaa atttatggat actgttattt tcacactata taattatgcc	3000
tctaatacgc gagaagaata tctacttctc aagcttttta aaactgctct ggaggaagaa	3060
ataaaatcaa aagtggacca ggtacaggac atagttactg gtaaccctac agtcatcaag	3120
atggtcgtca gcttcaatag aggtgcccg ggacagaaca ccctgcgcca actcctggct	3180
ccagtggtaa aagagatcat cgacgacaag tcgctgatta tcaacacaaa ccctgtagag	3240

- 26 -

gtgtacaagg cttgggtgaa ccaactagaa acacagactg gagaggccag caagttgcct 3300
tatgatgtga ccacagaaca agctctaaca taccagaag tgaaaaataa actggaggct 3360
tccattgaga acctgagaag ggtcaccgac aaagtcctga attctatcat ttcttcctt 3420
gatctactgc cttatggatt gaggtatata gccaaagtac tgaagaattc gatccatgag 3480
aaattccccg atgcaacaga agatgagcta ttaaagattg ttggaaacct cctgtactat 3540
cggtacatga atccagccat tgtagctcca gatggctttg atatcatcga catgacagct 3600
ggaggtcaga taaattctga ccaaaggaga aacttaggat cagtggccaa ggttcttcag 3660
cacgcagcct ccaacaagct gtttgaagga gaaaatgagc atctctcatc tatgaacaat 3720
tatttatcag agacgtatca ggaattcagg aaatatttca aagaagcatg taatgtccct 3780
gagccagaag agaagtttaa tatggacaaa tacacagacc tgggtgacagt cagcaaacca 3840
gtcatttata tttcaattga agaaatcatc agcacacact cactcctgtt ggaacaccag 3900
gatgcaattg cccctgagaa aaatgactta ctgagtgaat tgctggggtc gctgggagag 3960
gtgccaaccg tggaatcttt tcttggggaa ggagcagttg accccaatga ccctaacaag 4020
gcaaatacac taagtcagct ttcaaagacc gagatttctc ttgtcttgac aagcaaatat 4080
gacatagagg acggtgaagc tatagatagc cgaagcctca tgataaagac caagaagctg 4140
ataattgatg tgatccggaa ccagccaggg aacacattga cagaaatctt agagacacca 4200
gcaactgcgc aacaggaggt agaccatgcc acggacatgg tgagccgtgc aatgatagat 4260
tccaggactc cagaagaaat gaagcatagc caatctatga ttgaagatgc acagctgcct 4320
cttgagcaga agaagaggaa aatccagagg aatcttcgga cgttggaaca gactggacac 4380
gtgtcatccg aaaataaata ccaagacatt ctcaatgaga ttgccaagga tattcgaaat 4440
caaagaatct atcgtaagct tcgaaaagct gaattggcaa aacttcagca gaccctgaat 4500
gcacttaaca agaaggcagc attttatgaa gagcaaatca attattatga cacctacata 4560
aagacttggt tagacaactt aaaaagaaaa aatactcgga gatcaattaa actagatgga 4620
aaaggagaac ccaaaggggc gaagagagcg aagccagtga agtacactgc agcaaagctg 4680
catgagaaag gtgtcctgct agatatagat gatcttcaaa caaaccagtt taagaatggt 4740
acatttgata tcatagctac tgaagatgta ggcattttcg atgtaagatc aaaattcctt 4800
gggtgttgaga tggaagagg gcaactcaat attcaggatt tacttcagat gcaatatgaa 4860
ggagtagctg taatgaaaat gtttgataag gttaaagtga atgtaaacct tctcatatac 4920
ctgctgaaca agaagttcta tggaagtgta agtgccctaca gaaatttctt ggattctgta 4980

- 27 -

tcatctggat taggaaatga atttgtttta tttttttgtt tttaaacaatg attgaaatca 5040
 ctgcttataa atgtgtgatt tttttttaaat gaccaaaact gttctgaaga atgtacccag 5100
 gtgccttttt gctaatttga tactataata gaatgagaca taaaatgaat taatggaaac 5160
 atatccacac tgtactgtga tataggtact ctgattttaa actttggaca tcctgtgatc 5220
 tgtttttaag ttgggggggtg ggaaatttag ctgactaggg acaaacatgt aaacctattt 5280
 tcctatgaaa aaagttttta atgtcccact tgaataacgt aattcttcat agttttttta 5340
 atctatggat aaatggaaac ctaattattt gtaatgaatt atttagacag ttctaagccc 5400
 tgtcttctgg gagttatcaa ttttaaagag aacttttgtg caattcaa at gaagttttta 5460
 taagtaattg aaaatgacaa cacaataaca ctttctgtat aaaagtatat attttatgtg 5520
 atttattcct actaaatgaa agtgcactac tgcctcatgt aaagactctt gcacgcagag 5580
 cctttaagtg actaaggaac aacatagata gtgagcatag tccccacctc caccctcac 5640
 aatttatgtg aatacttcaa ttgtgcctct caattttttg taatgctaaa aaatcagtat 5700
 ctagatgggt tttaaatgta ttctctggaa attgttttat gtaaaataaa tgttacttaa 5760
 ttccatt 5767

<210> 16

<211> 3396

<212> DNA

<213> Homo sapiens

<400> 16

cttgcctgtt tcctggacaa acatcatgac attatcatca tagaccacag aaatcctcga 60
 cagctggatg cagaggcact gtgcaggtct atcagatcat caaaactctc agaaaacaca 120
 gttattgttg gtgtagtacg caggggtggat agagaagagt tgtccgtaat gcctttcatt 180
 tctgctggat ttacaaggag gtatgtagaa aaccccaaca tcatggcctg ctacaatgaa 240
 ctgctccagc tggagtttgg agaggtgcga tcacaactga aactcagggc ttgtaactca 300
 gtattcactg cattagaaaa cagtgaagat gcaattgaaa ttacaagcga agaccgtttt 360
 atacagtatg caaatcctgc atttgaaaca acaatgggct atcagtcagg tgaattaata 420
 ggaaggagt taggagaagt gcctataaat gaaaaaaagg ctgacttgct cgatactata 480
 aattcatgca tcaggatagg caaggagtgg caaggaattt actatgcaa aaagaaaaac 540
 ggagataata tacaacaaaa tgtgaagata atacctgtca ttggacaggg aggaaaaatt 600

agacactatg	tgtccattat	cagagtgtgc	aatggcaaca	ataaggctga	gaaaatatcc	660
gaatgtgttc	agtctgacac	tcgtacagat	aatcagacag	gcaaacataa	agacaggaga	720
aaaggctcac	tagacgtcaa	agctgttgcc	tcccgtgcaa	ctgaagtttc	cagccagaga	780
cgacactctt	ccatggcccg	gatacattcc	atgacaattg	aggcgcccat	caccaaggta	840
atcaatgtta	tcaatgctgc	ccaggaaagt	agtcccatgc	ctgtgacaga	agccctagac	900
cgtgtgctgg	aaattctaag	aaccactgag	ttatattcac	cacagtttgg	tgctaaagat	960
gatgatcccc	atgccaatga	ccttgttggg	ggcttaatgt	ctgatggttt	gcgaagacta	1020
tcagggaatg	aatatgttct	ttcaacaaaa	aacactcaaa	tggtttcaag	caatataatc	1080
actcccatct	cccttgatga	tgtcccacca	cggatagctc	gggccatgga	aaatgaggaa	1140
tactgggact	ttgatatttt	tgaactggag	gctgccaccc	acaataggcc	tttgatttat	1200
cttggtctca	aaatgtttgc	tcgctttgga	atctgtgaat	tcttacactg	ctccgagtca	1260
acgctaagat	catggttaca	aattatcgaa	gccaattatc	attcctccaa	tccttaccac	1320
aattctacac	attctgctga	tgtgcttcat	gccactgcct	attttctctc	caaggagagg	1380
ataaaggaaa	ctttagatcc	aattgatgag	gtcgctgcac	tcatcgcagc	caccattcat	1440
gatgtggatc	accctgggag	aaccaactcc	ttcctgtgta	atgctggaag	tgagctggcc	1500
attttgtaca	atgacactgc	tgtgctggag	agccaccatg	cggccttggc	cttccagctg	1560
accactggag	atgataaatg	caatatattt	aaaaacatgg	agagggaatga	ttatcggaca	1620
ctgcgccagg	ggattatcga	catggtctta	gccacagaaa	tgacaaagca	ctttgagcat	1680
gtcaacaaat	ttgtcaacag	catcaacaaa	cccttggcaa	cactagaaga	aaatggggaa	1740
actgataaaa	accaggaagt	gataaacact	atgcttagga	ctccagagaa	ccggacccta	1800
atcaaacgaa	tgctgattaa	atgtgctgat	gtgtccaatc	cctgcccagc	cctgcagtac	1860
tgcatcgagt	gggctgcacg	catttcggaa	gaatatTTTT	ctcagactga	tgaagagaag	1920
cagcagggct	tacctgtggt	gatgccagtg	tttgacagaa	atacctgcag	catccccaaa	1980
tcccaaattct	ctttcattga	ttacttcatc	acagacatgt	ttgatgcttg	ggatgccttt	2040
gtagacctgc	ctgatttaat	gcagcatctt	gacaacaact	ttaaatactg	gaaaggactg	2100
gacgaaatga	agctgcggaa	cctccgacca	cctcctgaat	agtgggagac	accaccaga	2160
gccctgaage	tttgttcctt	cggtcatttg	gaattcctga	gggcagccag	agctccttgg	2220
tcctttcagt	actaggcaga	acagcccccg	atctgcatag	cctgtgaaag	cccacgggga	2280
catcagtaac	cttctgcagc	caccatccaa	tgccattact	gtcaagtgag	acttggccac	2340

- 29 -

tgtagcctgg gectgctgca ggagctcttc agaaaggcac atgaggacca cggtttgcct 2400
 cagtttcttg taaaacacaa ggtctggagt gcccctgcaa agggatttga tggacttcct 2460
 gccagtgaca gagcatgtct attgcaaaca attctctcag ttacgttcag cacttaagaa 2520
 cggctaattg caataggatc tttagcaact ttttcacatc atagaagggtg caatcgctca 2580
 cttgggaaca ctactgagag tgacttctct tttaaaattg agtagcagat gaaaaattaa 2640
 aatttgaact tgattattaa tatcaattaa aatgttttat ttattttatt aaaagctcaa 2700
 tattttctat gaattcaaaa atacttcaga gccaaagcca acttcaaata ccgtgaccaa 2760
 atttacaatga ttcataattca ttatgcatta cttggtatac agacttattt tcataatgca 2820
 aattaataaa atgacacttt tactgcacta tagaaatatt catgtatggt aaacttttct 2880
 gattgaggct aactggaaaa agctgggggc gtattctaag tgctaaagaa ggctgcttct 2940
 actgtataga acccagggtc ctgaaacagc tctagccgcc taatgcactt cacaggtaac 3000
 tccccaagggt aaaactagac tctcttggtg gtctgcaaag aaaagttagg acttaacact 3060
 tttttctaaa attttataat tcaatttcca aaagtctact ctattttata ctgtttctac 3120
 aaaatattcc ttataaaaac aaagaacaaa aattgaatat ttaatgaatt gacattttat 3180
 aaccaacctg tttttatcta cggtggggaat ctttgatgcc agaaatttat aaagagggtc 3240
 tgtatcttca caccttgaat aagcataata ccataaaaaa tgacacttga catgtcaatg 3300
 tatttgatcat ttcattttta actcgtattt gtgggttttt tcccagataa aaatgaaatt 3360
 aaaccatttc tttttaagaa aaaaaaaaaa aaaaaa 3396

<210> 17

<211> 1406

<212> DNA

<213> Homo sapiens

<400> 17

cggcagggaa taaaggctca gggaccggca gttctactct agagcccacc agcctctcag 60
 agcctccggt gactggcctg tgtctccccc tggatggaca tgtggacggc gctgctcatc 120
 ctgcaagcct tgttgctacc ctccctggct gatggtgcca cccctgccct gcgctttgta 180
 gccgtgggtg actggggagg ggtccccaat gcccattcc acacggggccc ggaaatggcc 240
 aatgccaagg agatcgctcg gactgtgcag atcctgggtg cagacttcat cctgtctcta 300
 ggggacaatt ttacttcac tgggtgtgcaa gacatcaatg acaagagggt ccaggagacc 360

- 30 -

```

tttgaggacg tattctctga cegctccett cgcaaagtgc cctgggtacgt gctagccgga      420
aaccatgacc accttggcaa tgtctctgcc cagattgcat actctaagat ctccaagcgc      480
tggaacttcc ccagcccttt ctaccgcctg cacttcaaga tcccacagac caatgtgtct      540
gtggccattt ttatgctgga cacagtgaca ctatgtggca actcagatga cttcctcagc      600
cagcagcctg agaggccccg actaactgcc cgcacacagc tgtcctggct caagaaacag      660
ctggcggcgg ccaggaggga ctacgtgctg gtggctggcc actaccccgt gtgggtcata      720
gccgagcacg ggcctacca ctgcctggtc aagcagctac ggccactgct ggccacatac      780
ggggtcactg cctacctgtg cggccacgat cacaatctgc agtacctgca agatgagaat      840
ggcgtgggct acgtgctgag tggggctggg aatttcattg acccctcaaa gcggcaccag      900
cgcaagggtcc ccaacggcta tctgcgcttc cactatggga ctgaagactc actgggtggc      960
tttgcctatg tggagatcag ctccaaagag atgactgtca cttacatcga ggcctcgggc     1020
aagtccctct ttaagaccag gctgccgagg cgagccaggc cctgaactcc catgactgcc     1080
cagctctgag gcccgatctc cactgttggg tgggtggcct gccgggaccc tgctcacagg     1140
caggcttttc ctccaacctg tggcgctgca gcagggcagg aaggggaaac acagctgatg     1200
aactgtggtg ccacatgacc ttgtggcaca gatgccagta tgtgaacaca catggacatg     1260
tgtccagcac agtgtatgct cttggtctgg ctcaccgttt gctgagttcc ggggtgcaat     1320
gggggagggg gggagggaaa gcttcctcct aaatcaagca tctttctgtt actgatgttc     1380
aataaaagaa taggttgcca aggctg                                           1406

```

<210> 18

<211> 4198

<212> DNA

<213> Homo sapiens

<400> 18

```

ggcggagcga agagaaccgg tcgcggaat cctagcgcgc agcagcagca gcagcagcag      60
cagcagcagc agcagcagca gcagcaccgc catccgctgc gggagtccga gccggaacca     120
caccgaagta gctgcccttt cctcttctgt catctcaccg cccaccaca gaccgcgttc     180
cccgaggaaa ccggccgccc acgcccggag catcctcccc tgttgagcgg gcgctgacgg     240
accgggcggc atgatgcggc tgcgaggctc ggggatgctg cgggacctgc tcctgcggtc     300

```

gcccgcgcgc	gtgagcgcga	ctctgcggcg	ggcacagccc	ttggtcaccc	tgtgccggcg	360
tccccgaggc	gggggacggc	cggccgcggg	cccggctgcc	gccgcgcgac	tccacccgtg	420
gtggggcggg	ggcggctggc	cggcggagcc	cctcgcgcgg	ggcctgtcca	gctctccttc	480
ggagatcttg	caggagctgg	gcaaggggag	cacgcacccg	cagcccgggg	tgtcgccacc	540
cgctgccccg	gcggcgcccc	gcccccaagg	cggccccggg	gagacggacg	cgtttggtca	600
cagcgagggc	aaagagctgg	tggcctcagg	tgaaaataaa	ataaaacagg	gtctgttacc	660
tagcttgga	gatttgctgt	tctatacaat	tgctgaagga	caagagaaaa	tacctgttca	720
taaatttatt	acagcactca	aatctacagg	attgcgaacg	tctgatccca	ggttgaaaga	780
gtgtatggat	atgttaagat	taactcttca	aacaacatca	gatgggtgtca	tgctagacaa	840
agatcttttt	aaaaaatgtg	ttcagagcaa	cattgttttg	ttgacacaag	catttagaag	900
aaagtttgtg	attcctgact	ttatgtcttt	tacctcacac	attgatgagt	tatatgaaag	960
tgctaaaaag	cagtctggag	gaaagggtgc	agattatatt	cctcaactgg	ccaaattcag	1020
tcccgatattg	tgggggtgtg	ctgtttgtac	agtagatgga	cagaggcatt	ctactggaga	1080
taccaaagtt	cccttctgtc	ttcagtcctg	tgtaaaacct	ttgaaatatg	ccattgctgt	1140
taatgatctt	ggaactgaat	atgtgcatcg	atatgttgga	aaagagccga	gtggactaag	1200
attcaacaaa	ctatttttga	atgaagatga	taaaccacat	aatcctatgg	taaatgctgg	1260
agcaattggt	gtgacttcac	taataaagca	aggagtaa	aatgctgaaa	aatttgacta	1320
tgatcatgcag	tttttgaata	agatggctgg	taatgaatat	gttggtattca	gtaatgcaac	1380
gtttcagtct	gaaagagaaa	gtggagatcg	aaattttgca	ataggatatt	acttaaaaga	1440
aaagaagtgt	ttccagaag	gcacagacat	ggttggtata	ttagacttct	acttccagct	1500
gtgctccatt	gaagtgactt	gtgaatcagc	cagtgtgatg	gctgcgacac	tggttaatgg	1560
tggtttctgc	ccaattactg	gtgaaagagt	actgagccct	gaagcagttc	gaaatacatt	1620
gagtttgatg	cattcctgtg	gcatgtatga	cttctcaggg	cagtttgctt	tccatgttgg	1680
tcttcttgca	aatctggag	ttgctggggg	cattctttta	gttgtcccca	atgttatggg	1740
tatgatgtgc	tggtctcctc	ctctggataa	gatgggcaac	agtgttaagg	gaattcactt	1800
ttgtcacgat	cttgtttctc	tgtgtaattt	ccataactat	gataatttga	gacactttgc	1860
aaaaaaactt	gacctcgaa	gagaaggtgg	tgatcaaagg	gtaaagtcag	tgataaatct	1920
tttgtttgct	gcatatactg	gagatgtgtc	tgcaacttca	agatttgctt	tgtcagctat	1980
ggacatggaa	cagcgggact	atgattctag	aacagcactc	catgtagctg	ctgcagaggg	2040
tcatgttgaa	gttggttaaat	ttttgctgga	agcctgcaaa	gtaaaccctt	tccccaagga	2100

caggtggaat aacactccca tggatgaagc actgcacttt ggacaccatg atgtatttaa 2160
aattctccaa gaataccaag tccagtacac acctcaagga gattctgaca acgggaagga 2220
aaatcaaacc gtccataaga atcttgatgg attggtgtaa tggctc aaa tcccaagatt 2280
taaatacactt acctatttaa ttgtggaaaa tgattatgaa gaacatgtgt atttctatct 2340
ggtagtgatg tatattttac atttgtcatt tcagtgttac tggagttttc ttcattgtgc 2400
acacaggaca aatctgatct ctttgggaaa aaatagaaat aaaacaatct ccctccataa 2460
tgtgagcaat attacctcgt gcattgtata atttgatgta aaagaaatag ttaccaatgc 2520
tagcttgtgt ggtcttccat gatttatttg tgttttgtga attttcaatt tatggtgatg 2580
atctgctgat atgcatttat aaagtaagct ctggtgtaca gtctgtccaa atgggtcaag 2640
gttgccctta gaagcaaata gtgtgatttt caagacttca aatacaaatt tagtttaagt 2700
gtttgaacaa ctatatgcac ttacgggtgt gtgtttaaaa tgtctctctc tcaccctagc 2760
ttcatgatgt gactcttaaa aaactataat agttaacaac tgtagtaag atagaccaat 2820
tctgattaga ctttatcagg gaatctgttt aagatatgtt tggtgaccaa aacgtatgtg 2880
tgaatgtagt tataatgctt ttgaaaaatt ttcctttttc tatatcccct tagtccagcc 2940
tctcttctca gacatttagc tatctgcctc tttcctttag ctgggaaagt gagagctggc 3000
atactatgca gtttttatgt tttccatagt aagtcagaaa atgcctccta tttctggcat 3060
cagaactttg ccatttgtct acagaagacg aaccagagac aaaattacta agtataaatt 3120
agtcaagttt atcagtctaa aaagcgaagg gatgtgcaac tgcagctctt taagaagttt 3180
ttttttttta gcttctaggg taaagataaa ttcagaaatg ctctaagcta ccaaagttat 3240
tctgaaagta tgggaactgc tacaactaac aaacatttgt ttccaagcct gtcattaaga 3300
gtctgcatca agagatttgt cctccttggg ggaccaactgg atcattccag atttcttgtg 3360
atttttctat tgtgtaattc ttggtgggct ctgtagttta ataataagaa aaaggccatt 3420
tcattttaaa ttgtgacctt taattctttg tcttgggttg gtaattcagg attcatttgg 3480
aaagtgggta aaaggggctt caaaaaacgg atagaacagg attttctagg agttacacat 3540
acattttatc ctgtcatacc tcgagataaa gtggcatgtt agtgaggagt tctgatatta 3600
agcacacaca cacatgcaca caaatggact tctctgaagc tgtgttttagt gaaatgagct 3660
caagtacatg aatgttagtt gttatcacat acagcaaatt cctttttttt tctttttcta 3720
tgagcacact ctgctgcttc taaactttac atgcctgatg gcaccttact ccagcagcct 3780
ccaggtgctt tcattttcac ttccagtcta agccagtggc tcctgccact gccctcccat 3840

- 33 -

tacctagatg	gcacctcctt	tgggtgaaacc	acggccaatg	ttccttagct	gcaccaggcc	3900
cgaagctggt	cccatgcttg	agcttccatg	gggaggatgc	tgagtgagca	gtttcctacg	3960
ccgtggatct	agcaagccat	ggagacaggt	agcatttgta	agatgctgca	caggagcagc	4020
attatcccca	aagatattac	agggtagaca	cgtttttaact	gaaatcaatc	aagataactt	4080
tattcaaaga	gcagcccgtt	ttgtgtgact	aaaatgaaac	aagacagttg	aattgtgtga	4140
cttgaagatt	accaatgatt	ttgaggcttt	tctataataa	aaagagggttc	taaccatt	4198

<210> 19

<211> 1635

<212> DNA

<213> Homo sapiens

<400> 19

aaaggaagag	aaagggagag	agggagagaa	gagggagaga	gcagagagac	ctcaccgaga	60
gagctgcaaa	accagcctgg	aaaaattaga	gtattaccta	acattagtga	aaaataaagg	120
tactttcttg	agaagccctt	ggaccatttc	tgcctcctgg	agttctgaac	ttttcactca	180
ctgcctatta	attaatgtta	agcctgcaaa	gaatggagtt	gtcctggata	tttggccaaa	240
aaaaaaaaatgt	atccacaaac	agggacgtaa	tcaggcaggg	agcctcggtta	agaagttttg	300
ttcttgtcct	aggagtgatg	agagatcact	gaaggattta	gagaggggct	gtatcatcag	360
gcttgggttc	caaagcctca	ctgagagagt	tggggagctg	actgatgtca	gatgctcgtg	420
cagccgcccc	gtagggcctg	tatttcctcc	atggtgcctc	actgcagcac	cgagcttgca	480
aaagatcctc	tctcttttatg	ggaatttcaa	aacagaagca	aaatagcacc	ggggcttaaa	540
gcattcttgg	gaatttcctt	gtctttccct	ctaaataatc	agcatgtaaa	ttgcaaaaaa	600
aaaaaaaaaaaa	aaaaaagaca	cgggcccaca	agggagcgct	cagtttcagg	ctctttgctt	660
tccttcctcc	cgaggctctc	tggcccttac	ccagcctgaa	aacaaaaagt	gtgaggggga	720
gggtaggaag	gtagttcaag	cagggaatg	ctgagcctgg	gaagaaaaca	acagccttgt	780
ttagggcact	gtggcttacg	taactaaatt	gtgccagtt	tccacctggc	caggggcctg	840
gagtgaatgc	tgaagatgca	aaggtagagg	ctgccagaaa	agccaggaaa	ttgctggcaa	900
gaaaggccag	tgggtggggtg	caggagtggg	aggaaggctg	ggaaatgcgg	ctgagtcaca	960
tctccagaag	ccccccatca	tcaccctagt	ggctcttctg	ctggcaggcg	cctcatgaag	1020
acctgacca	aagttttcaa	aactctgcgg	tttctcaacc	ctcctctggt	aatccatagt	1080

- 34 -

actccccgc ctccacttgc cagcctcgtg attccttcat ggacacatag ctcagttccc 1140
 ataaaagggc tggtttgccg cgtgggggag tggagtggga caggtatata aaggaagtac 1200
 agggcctggg gaagaggccc tgtctaggta gctggcacca ggagccgtgg gcaagggaag 1260
 aggccacacc ctgccctgct ctgctgcage cagaatgggt gtgaaggcgt ctcaaacagg 1320
 tatctgggct agccaagggt aatccatcag agttgtgggt tttcaggccc agacagcccg 1380
 cagagccatc tgcctgctgg gtgagggact aagggagtgg gcagaggggg aggagaagca 1440
 gagccagggg agggactgag gctgcaacca ggagggtggg gtgggggagt ggggtctcagt 1500
 tgcttggggg agggagcagg gcggaagggc aggatgcact tgcaggggtc tcctcctgga 1560
 tttctcttca ggctttgtgg tcctggtgct gctccagtgc tgtgagtaat ccctccacct 1620
 ccacttttaa gtcca 1635

<210> 20

<211> 1850

<212> DNA

<213> Homo sapiens

<400> 20

gaatcgcctg ccacaggtgt ctgcaattga actccaaggt gcagaatggt ttggaaagta 60
 gctgtattcc tcagtgtggc cctgggcatt ggtgccgttc ctatagatga tcctgaagat 120
 ggaggcaagc actgggcagt gatcgtggca ggttcaaagc gctggtataa ttataggcac 180
 caggcagacg cgtgccatgc ctaccagatc attcaccgca atgggattcc tgacgaacag 240
 atcgttgtga tgatgtacga tgacattgct tactctgaag acaatcccac tccaggaatt 300
 gtgatcaaca ggccaatgg cacagatgtc tatcagggag tcccgaagga ctacactgga 360
 gaggatgtta cccacaaaaa tttccttgcgt gtgttgagag gcgatgcaga agcagtgaag 420
 ggtataggat ccggcaaagt cctgaagagt ggcccccagg atcacgtgtt catttacttc 480
 actgaccatg gatctactgg aatactggtt tttcccaatg aagatcttca tgtaaaggac 540
 ctgaatgaga ccatccatta catgtacaaa cacaaaatgt accgaaagat ggtgttctac 600
 attgaagcct gtgagtctgg gtccatgatg aaccacctgc cggataacat caatgtttat 660
 gcaactactg ctgccaaccc cagagagtcg tcctacgcct gttactatga tgagaagagg 720
 tccacgtacc tgggggactg gtacagcgtc aactggatgg aagactcgga cgtggaagat 780

- 35 -

ctgactaaag agaccctgca caagcagtac cacctggtaa aatcgcacac caacaccage 840
 cacgtcatgc agtatggaaa caaaacaatc tccaccatga aagtgatgca gtttcagggt 900
 atgaaacgca aagccagttc tcccgcccc ctacctccag tcacacacct tgacctcacc 960
 cccagccctg atgtgcctct caccatcatg aaaaggaaac tgatgaacac caatgatctg 1020
 gaggagtcca ggcagctcac ggaggagatc cagcggcatc tggatgccag gcacctcatt 1080
 gagaagtcag tgcgtaagat cgtctccttg ctggcagcgt ccgaggctga ggtggagcag 1140
 ctctgtccg agagagcccc gctcacgggg cacagctgct acccagagge cctgctgcac 1200
 ttccggaccc actgcttcaa ctggcactcc cccacgtacg agtatgcgtt gagacatttg 1260
 tacgtgctgg tcaacctttg tgagaagccg tatccgcttc acaggataaa attgtccatg 1320
 gaccacgtgt gccttgggtca ctactgaaga gctgcctcct ggaagctttt ccaagtgtga 1380
 gcgccccacc gacatgtgtg ctgatcagag actggagagg tggagtgaga agtctccgct 1440
 gctcggggccc tcctgggggag cccccgctcc agggctcgtt ccaggacctt cttcacaaga 1500
 tgacttgctc gctgttacct gcttccccag tcttttctga aaaactacaa attaggggtg 1560
 gaaaagctct gtattgagaa gggcatatt tgctttctag gaggtttgtt gttttccctg 1620
 ttagttttga ggagcaggaa gctcatgggg gcttctgtag cccctctcaa aaggagtctt 1680
 tattctgaga atttgaagct gaaacctctt taaatcttca gaatgatttt attgaagagg 1740
 ggcgcaagcc ccaaattggaa aactgttttt agaaaatatg atgatttttg attgcttttg 1800
 tatttaattc tgcaggtggt caagtcttaa aaaataaaga ttataacag 1850

<210> 21

<211> 1575

<212> DNA

<213> Homo sapiens

<400> 21

agaaccgcga cctccgcaac cttgagcggc atccgtggag tgcgcctgca gctacgaccg 60
 cagcaggaaa gcgcgcgcgg ccaggcccag ctgtggccgg acagggactg gaagagagga 120
 cgcggtcgag taggtgtgca ccagccctgg caacgagagc gtctaccccg aactctgctg 180
 gccttgaggt ggggaagccg gggagggcag ttgaggaccc cgcggaggcg cgtgactggt 240
 tgagcgggca ggccagcctc cgagccgggt ggacacaggt tttaaaacat gaatcctaca 300
 ctcacccctg ctgccttttg cctgggaatt gcctcagcta ctctaacatt tgatcacagt 360

- 36 -

```

ttagaggcac agtggaccaa gtggaaggcg atgcacaaca gattatacgg catgaatgaa      420
gaaggatgga ggagagcagt gtgggagaag aacatgaaga tgattgaact gcacaatcag      480
gaatacaggg aagggaaaca cagcttcaca atggccatga acgccttttg agacatgacc      540
agtgaagaat tcaggcaggt gatgaatggc tttcaaaacc gtaagcccag gaaggggaaa      600
gtgttccagg aacctctgtt ttatgaggcc ccagatctg tggattggag agagaaaggc      660
tacgtgactc ctgtgaagaa tcagggtcag tgtggttctt gttgggcttt tagtgetact      720
ggtgctcttg aaggacagat gttccggaaa actgggaggc ttatctcact gagtgagcag      780
aatctggtag actgctctgg gcctcaaggc aatgaaggct gcaatggtgg cctaattgat      840
tatgctttcc agtatgttca ggataatgga ggcttgact ctgaggaatc ctatccatat      900
gaggcaacag aagaatcctg taagtacaat cccaagtatt ctgttgctaa tgacaccggc      960
tttgtggaca tccctaagca ggagaaggcc ctgatgaagg cagttgcaac tgtggggccc     1020
atctctgttg ctattgatgc aggtcatgag tccttcctgt tctataaaga aggcatttat     1080
tttgagccag actgtagcag tgaagacatg gatcatggtg tgctggtggt tggctacgga     1140
tttgaaagca cagaatcaga taacaataaa tattggctgg tgaagaacag ctgggggtgaa     1200
gaatggggca tgggtggcta cgtaaagatg gccaaagacc ggagaaacca ttgtggaatt     1260
gcctcagcag ccagctaccc cactgtgtga gctggtggac ggtgatgagg aaggacttga     1320
ctgggggatgg cgcatgcatg ggaggaattc atcttcagtc taccagcccc cgctgtgtcg     1380
gatacacact cgaatcattg aagatccgag tgtgatttga attctgtgat attttcacac     1440
tggtaaatgt tacctctatt ttaattactg ctataaatag gtttatatta ttgattcact     1500
tactgacttt gcattttcgt ttttaaagg atgtataaat ttttacctgt ttaaataaaa     1560
tttaatttca aatgt                                           1575

```

<210> 22

<211> 737

<212> DNA

<213> Homo sapiens

<400> 22

```

ccagctcaag actttgctct ccaccaggca gaagatgaca gactgtgaat ttggatatat      60
ttacaggctg gctcaggact atctgcagtg cgtectacag ataccacaac ctggatcagg     120

```


- 37 -

tccaagcaaa	acgtccagag	tgctacaaaa	tgttgcgttc	tcagtccaaa	aagaagtgga	180
aaagaatctg	aagtcattgt	tggacaatgt	taatgtttgt	tccgtagaca	ctgccagaac	240
actattcaac	caagtgatgg	aaaaggagtt	tgaagacggc	atcattaact	ggggaagaat	300
tgtaaccata	tttgcatttg	aaggtattct	catcaagaaa	cttctacgac	agcaaattgc	360
cccggatgtg	gatacctata	aggagatttc	atattttgtt	gcggagttca	taatgaataa	420
cacaggagaa	tggataaggc	aaaacggagg	ctgggaaaat	ggctttgtaa	agaagtttga	480
acctaaatct	ggctggatga	cttttctaga	agttacagga	aagatctgtg	aaatgctatc	540
tctcctgaag	caatactgtt	gaccagaaag	gacactccat	attgtgaaac	cggcctaatt	600
tttctgactg	atatggaaac	gattgccaac	acatacttct	acttttaaata	aaacaacttt	660
gatgatgtaa	cttgaccttc	cagagttatg	gaaattttgt	cccatgtaa	tgaataaatt	720
gtatgtattt	ttctcta					737

<210> 23

<211> 2637

<212> DNA

<213> Homo sapiens

<400> 23

gagagcactg	cagcagcaat	gacggagggc	acgtgtctgc	ggcgccgagg	gggcccctac	60
aagaccgagc	ccgccaccga	cctcggccgc	tggecactca	actgcgagag	gggcccggcag	120
acgtggacct	acctgcagga	cgagcgcgcc	ggccgcgagc	agaccggcct	ggaagcctac	180
gccctggggc	tggacaccaa	gaattacttt	aaggacttgc	ccaaagccca	caccgccttt	240
gagggggctc	tgaacgggat	gacattttac	gtggggctgc	aggctgagga	tgggcactgg	300
acgggtgatt	atggtggccc	acttttcctc	ctgccaggcc	tcctgatcac	ttgccacgtg	360
gcacgcatec	ctctgccagc	cggatacaga	gaagagattg	tgcggtacct	gcggtcagtg	420
cagctccctg	acggtggctg	gggcctgcac	attgaggata	agtccaccgt	gtttgggact	480
gcgctcaact	atgtgtctct	cagaattctg	ggtgttgggc	ctgacgatcc	tgacctggta	540
cgagcccgga	acattcttca	caagaaaggt	ggtgctgtgg	ccatcccctc	ctgggggaag	600
ttctggctgg	ctgtcctgaa	tgtttacagc	tgggaaggcc	tcaataccct	gttcccagag	660
atgtggctgt	ttctgactg	ggcaccggca	caccctcca	cactctgggtg	ccactgccgg	720
caggtgtacc	tgcccatgag	ctactgctac	gccgttcggc	tgagtgcgcg	ggaagacccg	780

ctgggtccaga gcctccgcca ggagctctat gtggaggact tcgccagcat tgactggctg	840
gcgcagagga acaacgtggc ccccgacgag ctgtacacgc cgcacagctg gctgctccgc	900
gtggtatatg cgctcctcaa cctgtatgag caccaccaca gtgcccacct gcggcagcgg	960
gccgtgcaga agctgtatga acacattgtg gccgacgacc gattcaccaa gagcatcagc	1020
atcggcccga tctcgaaaac catcaacatg cttgtgcgct ggtatgtgga cgggcccgc	1080
tccactgcct tccaggagca tgtctccaga atcccggact atctctggat gggccttgac	1140
ggcatgaaaa tgcagggcac caacggctca cagatctggg acaccgcatt cgcctccag	1200
gctctgcttg aggcgggcgg gcaccacagg ccgagtttt cgtcctgcct gcagaaggct	1260
catgagttcc tgaggctctc acagggtcca gataaccctc ccgactacca gaagtactac	1320
cgcagatgc gcaaggggtg cttctccttc agtacgctgg actgcggctg gatcgtttct	1380
gactgcacgg ctgaggcctt gaaggctgtg ctgctcctgc aggagaagtg tcccatgtc	1440
accgagcaca tcccagaga acggtcttgc gatgctgtgg ctgtgctgct gaacatgaga	1500
aatccagatg gagggttcgc cacctatgag accaagcgtg gggggcactt gctggagctg	1560
ctgaaccctt cggaggtctt cggggacatc atgattgact acacctatgt ggagtgcacc	1620
tcagccgtga tgcaggcgtt taagtatttc cacaagcgtt tcccggagca cagggcagcg	1680
gagatccggg agaccctcac gcagggttta gagttctgtc ggccggcagca gagggccgat	1740
ggctcctggg aaggctcctg gggagtttgc ttcacctacg gcacctgggt tggcctggag	1800
gccttcgcct gtatggggca gacctaccga gatgggactg cctgtgcaga ggtctcccgg	1860
gcctgtgact tcctgctgtc ccggcagatg gcagacggag gctgggggga ggactttgag	1920
tcctgcgagg agcggcggtta tttgcagagt gccagtcctc agatccataa cacatgctgg	1980
gccatgatgg ggctgatggc cgttcggcat cctgacatcg aggcccagga gagaggagtc	2040
cgggtgtctac ttgagaaaca gctcccctaat ggcgactggc cgcaggaaaa cattgctggg	2100
gtcttcaaca agtcctgtgc catctcctac acgagctaca ggaacatctt tcccatctgg	2160
gcctcgggc gcttctccca gctgtaccct gagagagccc ttgctggcca cccctgagaa	2220
catgcctacc tgctgggtgc cgtctgtgcg ttccatggcc ttcaagtcac aggacgcagc	2280
gattcccatt ccctgcctc ttcggtgtta ttacacaggc aggacttcag tgtcagtatc	2340
cctgccttca gtcttcttta gaaatcacat ctgtgttcaa tccattgttt agagggagtg	2400
tatttttcct gtccacgaa gaggactttt tgttcacaat tggatcaciaa tgcagaggag	2460
tctgttcctc ccccgctggc ttctcggtgc tgggaggggtg acctgtccca gatgactcat	2520

- 39 -

caccctgaca tgctcttgac aaaggacacc accaagagga gatggcagct gtaccggtgc 2580
 agcctctgtc tgagggggat atttgccctca gtgtgattaa aaatcagtca tgaaaga 2637

<210> 24

<211> 1807

<212> DNA

<213> Homo sapiens

<400> 24

tctgtggccg gaggctgac agtgttctag aacagatcag acattttgta atgatgcctg 60
 aaataaacac taaccacctc gacaagcaac aggttcaact cctggcagag atgtgtatcc 120
 ttattgatga aaatgacaat aaaattggag ctgagaccaa gaagaattgt cacctgaacg 180
 agaacattga gaaaggatta ttgcatcgag ctttttagtgt cttcttattc aacaccgaaa 240
 ataagcttct gctacagcaa agatcagatg ctaagattac ctttccaggt tgttttacga 300
 atacgtgttg tagtcatcca ttaagcaatc cagccgagct tgaggaaagt gacgcccttg 360
 gagtgaggcg agcagcacag agacggctga aagctgagct aggaattccc ttggaagagg 420
 ttctccaga agaaattaat tatttaacac gaattcacta caaagctcag tctgatggta 480
 tctgggggtga acatgaaatt gattacattt tgttggtgag gaagaatgta actttgaatc 540
 cagatcccaa tgagattaaa agctattggt atgtgtcaaa ggaagaacta aaagaacttc 600
 tgaaaaaagc agccagtggg gaaattaaga taacgccatg gtttaaaatt attgcagcga 660
 cttttctctt taaatggtgg gataacttaa atcatttgaa tcagtttggt gaccatgaga 720
 aaatatacag aatgtgaata tgtaggtaaa tgattacaga aaaatttatg tgcttaacaa 780
 acttagaatg actttttcct tttaaattta gttctatcat taatttatca ttaaatttag 840
 ttctatcatt tgggtactatc attaatgtat tataaaactt gtgtggaaaa aactaactta 900
 taattttgta tcacacaccc tggatatgtg ttctgtttct aagcgacatt tgtgagagat 960
 tattgtaaaa tgagagcgag aaataaaact taatttaatc tttgcagata catacttatg 1020
 ggaaatttga acaaatgagt gaaactctgt ttttagtagg ccgtgataaa catttccgga 1080
 gcacttgcag aggacttgct atttgccagg tgctttatgt atcattaaat ttttctcata 1140
 gttcagaaaa atgtgcaaag gaaactattg tctcgctcct tcaaaacagt ctttaattaac 1200
 tttcatatta gcagattaaa ctagcagagc aaggttcaaa ttaaatgata tgaccetaat 1260
 ttgtatcatt ctgagttgat tgtgtggttt attcattctg aaacatgttg atacttacag 1320

- 40 -

tcaccgactg cttttgataa gtgatattga ttaggttgaa tcttcttgta aatagtattt 1380
 accagttagc aaagtctgtg ttttcagaat tacagtgage acagaggtgt tcataaaatg 1440
 ggaattgagt ccactcgggt aagagttgct taaacttgac actgttgaca tttgggctgg 1500
 ataaaacccc tgtggtgggg tctgtgctgt gcattgcagg atggtgagca gcgtccctct 1560
 catgtgacac ccacagttat gcgggatgtt gccagatgcc cctagggaca gagtcaaccc 1620
 ccaactgagg accactgtct acagagtcag gaaatattgt agggagaaaa aaataacaac 1680
 aacaaaggcc tatattaatg ttaaataagag gagattatgg aatgtgtata ttaatgttaa 1740
 aaattattcc ttattcaatg tattttttatc aaatcgatag atatctcaga tttgaaactc 1800
 aagacag 1807

<210> 25

<211> 1401

<212> DNA

<213> Homo sapiens

<400> . 25

cgtattgctc ggcccgggga gtttcgcccc ctgcccggtt ccgcggcgcg gaggatggcg 60
 tggaacggc tgggcgcgct ggtgatgttc cctctacaga tgatctatct ggtggtgaaa 120
 gcagccgtcg gactggtgct gcccgccaag ctgcgggacc tgtcgcggga gaacgtcctc 180
 atcaccggcg gcgggagagg catcgggcgt cagctcgccc gcgagttcgc ggagcgcggc 240
 gccagaaaga ttgttctctg gggccggact gagaaatgcc tgaaggagac gacggaggag 300
 atccggcaga tgggcactga gtgccattac ttcatctgtg atgtgggcaa ccgggaggag 360
 gtgtaccaga cggccaaggc cgtccgggag aaggtgggtg acatcaccat cctggtgaac 420
 aatgccgccg tgggccatgg gaagagccta atggacagtg atgatgatgc cctcctcaag 480
 tcccaacaca tcaacaccct gggccagttc tggaccacca aggccttcct gccgcgtatg 540
 ctggagetgc agaatggcca catcgtgtgc ctcaactccg tgctggcact gtctgccatc 600
 cccggtgcca tcgactactg cacatccaaa gcgtcagcct tcgccttcat ggagagcctg 660
 accctggggc tgctggactg tccgggagtc agcgccacca cagtgtgtgc ctccacacc 720
 agcaccgaga tgttccaggg catgagagtc aggtttccca acctctttcc ccactgaag 780
 ccggagacgg tggcccgagg gacagtggaa gctgtgcagc tcaaccaggc cctcctcctc 840

- 41 -

ctcccatgga caatgcatgc cctcgttatc ttgaaaagca tacttccaca ggctgcactc 900
gaggagatcc acaaattctc aggaacctac acctgcatga acactttcaa agggcggaca 960
tagagacagg atgaagacat gcttgaggag ccacggagtt tggggggccac agcacctggg 1020
cacacacccg agcacctgtc cattggcatg cttctgctgg gtgagcagga cagctcctgt 1080
ccccagcgaa gaatccgget gccctgggc cagtcccagg acctttgcac aggactgatg 1140
ggtgtaactg acccccacag ggaggcagga aaacagccag aagccacctt gacacttttg 1200
aacatttcca gttctgtaga gtttattgtc aattgcttct caagtctaac cagcctcagc 1260
agtgtgcata gaccatttcc aggagggtct gtcccagat gctctgcctc ccgttccaaa 1320
accactcat cctcagcttg cacaaactgg ttgaacggca ggaatgaaaa ataaagagag 1380
atggcttttg tgaaaaaaaa a 1401

<210> 26

<211> 2497

<212> DNA

<213> Homo sapiens

<400> 26

gggcgcgag gctccccgcc gctcgctgct ccccggcccg cgccatgcc tcctacacgg 60
tcaccgtggc cactggcagc cagtgggttcg ccggcactga cgactacatc tacctcagcc 120
tcgtgggctc ggccgggctgc agcgagaagc acctgctgga caagcccttc tacaacgact 180
tcgagcgtgg cgcggtggat tcatacgacg tgactgtgga cgaggaactg ggcgagatcc 240
agctggtcag aatcgagaag cgcaagtact ggctgaatga cgactggtac ctgaagtaca 300
tcacgctgaa gacgccccac ggggactaca tcgagttccc ctgctaccgc tggatcaccc 360
gcgatgtcga ggttgctcctg agggatggac gcgcaaagtt ggcccgagat gaccaaattc 420
acattctcaa gcaacaccga cgtaaagaac tggaaacacg gcaaaaacaa tatcgatgga 480
tggagtggaa ccctggcttc cccttgagca tcgatgccaa atgccacaag gatttaccce 540
gtgatatcca gtttgatagt gaaaaaggag tggactttgt tctgaattac tccaaagcga 600
tggagaacct gttcatcaac cgcttcatgc acatgttcca gtcttcttgg aatgacttcg 660
ccgactttga gaaaatcttt gtcaagatca gcaacactat ttctgagcgg gtcataatc 720
actggcagga agacctgatg tttggctacc agttcctgaa tggctgcaac cctgtgttga 780
tccggcgctg cacagagctg cccgagaagc tcccggtgac cacggagatg gtagagtgca 840

- 42 -

gcctggagcg gcagctcagc ttggagcagg aggtccagca agggaaacatt ttcacgtgg	900
actttgagct gctggatggc atcgatgcca aaaaaacaga cccctgcaca ctccagttcc	960
tggcgcgtcc catctgcttg ctgtataaga acctggccaa caagattgtc cccattgcca	1020
tccagctcaa ccaaattccc ggagatgaga accctatttt cctccccttcg gatgcaaaat	1080
acgactggct tttggccaaa atctgggtgc gttccagtga ctccacgtc caccagacca	1140
tcacccacct tctgogaaca catctggtgt ctgaggtttt tggcattgca atgtaccgcc	1200
agctgcctgc tgtgcacccc attttcaagc tgctgggtggc acacgtgaga ttcaccattg	1260
caatcaaac caaggcccg gagcagctca tctgcgagtg tggcctcttt gacaaggcca	1320
acgccacagg gggcggtggg cacgtgcaga tgggtgcagag ggccatgaag gacctgacct	1380
atgcctccct gtgctttccc gaggccatca aggcccgggg catggagagc aaagaagaca	1440
tcccctacta cttctaccgg gacgacgggc tcctggtgtg ggaagccatc aggacgttca	1500
cggccgaggt ggtagacatc tactacgagg gcgaccaggt ggtggaggag gaccgcgagc	1560
tgcaggactt cgtgaacgat gtctacgtgt acggcatgcg gggccgcaag tcctcagget	1620
tccccaagtc ggtcaagagc cgggagcagc tgtcggagta cctgacgtg gtgatcttca	1680
cgcctccgc ccagcacgcc gcggtcaact tcggccagta cgactggtgc tcctggatcc	1740
ccaatgcgcc cccaaccatg cgagccccgc caccgactgc caagggcggtg gtgaccattg	1800
agcagatcgt ggacacgctg cccgaccgcg gccgctcctg ctggcatctg ggtgcagtgt	1860
gggcgctgag ccagttccag gaaaacgagc tgttcctggg catgtaccca gaagagcatt	1920
ttatcgagaa gcctgtgaag gaagccatgg cccgattccg caagaacctc gaggccattg	1980
tcagcgtgat tgctgagcgc aacaagaaga agcagctgcc atattactac ttgtccccag	2040
accggattcc gaacagtgtg gccatctgag cacactgcca gtctcactgt ggggaaggcca	2100
gctgccccag ccagatggac tcagcctgc ctggcaggct gtctggccag gcctcttgge	2160
agtcacatct cttcctccga ggccagtacc ttccatttta ttctttgatc ttcagggaac	2220
tgcatagatt gtatcaaagt gtaaacacca tagggacca ttctacacag agcaggactg	2280
cacaggcgtc ctgtcacac ccagctcagc atttccacac caagcagcaa cagcaaatca	2340
cgaccactga tagatgteta ttcttggttg agacatggga tgattatttt ctgttctatt	2400
tgtgcttagt ccaattcctt gcacatagta ggtacccaat tcaattacta ttgaatgaat	2460
taagaattgg ttgccataaa aataaatcag ttcattt	2497

- 43 -

<210> 27

<211> 2125

<212> DNA

<213> Homo sapiens

<400> 27

gatcccccg	gctgcaggaa	ttcccgggtc	gacccacgcg	tccggtgcgg	acgggcgcg	60
accacctcca	ggggctaagt	gatggatctt	gtactccgtg	ttgcagatta	ctattttttt	120
acaccatacg	tgtatccagc	cacatggcca	gaagatgaca	tcttccgaca	agctattagt	180
cttctgattg	taacaaatgt	tggtgcttac	atcctttatt	tcttctgtgc	aacactgagc	240
tattattttg	tcttcgatca	tgcattaatg	aaacatccac	aattttttaa	gaatcaagtc	300
cgtcgagaga	ttaagtttac	tgtccaggca	ttgccatgga	taagtattct	tactgttgca	360
ctgttcttgc	tggagataag	aggttacagc	aaattacatg	atgacctagg	agagtttcca	420
tatggattgt	ttgaacttgt	cgtagtata	atatctttcc	tctttttcac	tgacatgttc	480
atctactgga	ttcacagagg	ccttcatcat	agactgggat	ataagcgcct	acataaacct	540
caccatattt	ggaagattcc	tactccattt	gcaagtcatg	cttttcaccc	tattgatggc	600
tttcttcaga	gtctacctta	ccatatatac	ccttttatct	ttcattaca	caagggtggt	660
tatttaagtc	tgtacatctt	ggttaatatc	tggacaattt	ccattcatga	cggtgatttt	720
cgtgtccccc	aatctttaca	gccatttatt	aatggctcag	ctcatcatac	agaccaccat	780
atgttctttg	actataatta	tggacaatat	ttcactttgt	gggataggat	tggcggctca	840
ttcaaaaatc	cttcatcctt	tgaggggaag	ggaccgctca	gttatgtgaa	ggagatgaca	900
gagggaaagc	gcagcagccc	ttcaggaaat	ggctgtaaga	atgaaaaatt	attcaatgga	960
gagttttaca	agactgaata	gattattgcc	cagttattct	taagtaagga	caaagaagga	1020
aatatcatcg	tatttctttt	ttttaataag	gaaaaaataa	tctccataca	gtcaagatac	1080
atagtaaattg	gtatcatttg	gaaatcagca	tcgtgggcac	tgctgaggaa	tgatcctagt	1140
ggtaggtcag	aagaagatgc	tgtgaacacc	aggactttaa	tcttatgctt	aaaatgccag	1200
atgttgttcg	ggccccaact	tgtattttcta	gcagcagatc	tgtagtgtgt	atagcctcaa	1260
caacaatttt	aaataagatg	gagaataaat	tattgagggg	actaggctat	atgcatttgc	1320
cttcatccac	ccatgtttat	taagaatcat	tgtgcttaat	aataccaaga	ctaagcacca	1380
taaccaagaa	atactaattgt	aaagattggt	tcttgtttca	ggaatgggta	attcttcaac	1440

- 44 -

gttggtatga taatgataac ttgttttgac ttgaataaag tactacatca gtgtggaaaa 1500
 aaattctgat acattagcag ctatgtaaat gacctaatg atagcagggtg taataagact 1560
 atcgtcttcc tacacatagg aggctcattc tctggacaca ctatcaccta ttacatttta 1620
 ctgattaaca aataaattgg aatttaaaaa tatcgatatc accatgattt aatccagatc 1680
 tgggattatg tagctaaaca ttgtgatgat tattatttaa aaccattatt taataagagt 1740
 aaaaatatgt gaatctggat atatttaaaa aaagaaattt gattgcccag ataatatatt 1800
 aggcactact gatttttttag ttaaattgat gcactacact tttgatgttt gaagttacaa 1860
 cctgtaattt ttttgtaaag gaaataattg ccaaatacct aggccattg ctgacgatta 1920
 gttctaaaat cttattcctc ctcttctccc ctacttttc cctacttcct ctgcaaaaag 1980
 atttaacaaa tacattcata aggaaatgtg tgttgtaaca aatatattgc aaaaacatag 2040
 tttgtaaagg cattctataa gctatttatg taaaatcaat aaaagttgat cataattaaa 2100
 ctgtaaaaaa aaaaaaaaaag gcggc 2125

<210> 28

<211> 2685

<212> DNA

<213> Homo sapiens

<400> 28

caggcgtgtc ccagggggag ccccgctctg cagccctgtg cgccgtagag agctggactt 60
 aggctggcag catggccgag ttcaggggtca ggggtgtccac cggagaagcc ttcggggctg 120
 gcacatggga caaagtgtct gtcagcatcg tggggaccog gggagagagc cccccactgc 180
 ccctggacaa tctcggcaag gagttcactg cgggcgctga ggaggacttc caggtgacgc 240
 tcccggagga cgtagggcga gtgctgctgc tgcgcgtgca caaggcgccc ccagtgtctgc 300
 ccctgctggg gccctggcc ccggatgcct gggttctgcg ctgggtccag ctgacaccgc 360
 cgcggggcgg ccacctcctc tccccctgct accagtggct ggagggggcg gggaccctgg 420
 tgctgcagga gggtagagcc aaggtgtcct gggcagacca ccacctgtg ctccagcaac 480
 agcgccagga ggagcttcag gcccggcagg agatgtacca gtggaaggct tacaaccag 540
 gttggcctca ctgcctggat gaaaagacag tggaagactt ggagctcaat atcaaatact 600
 ccacagccaa gaatgccaac ttttatctac aagctggctc tgcttttgca gagatgaaaa 660
 tcaaggggtt gctggaccgc aaggggctct ggaggagtct gaatgagatg aaaaggatct 720

tcaacttccg gaggacccca gcagctgagc acgcatttga gcaactggcag gaggatgcct	780
tcttcgcctc ccagttcctg aatggtctca accctgtcct gatccgccgc tgtcactacc	840
tcccaaagaa cttccccgtc actgatgcc a tggtggcctc attggtgggt cctgggacca	900
gcttgcaggc tgagctagag aagggctccc tgttcttggt ggatcacggc atcctctctg	960
gcatccagac caatgtcatt aatgggaagc cgcagttctc tgcggcccca atgaccctgc	1020
tataccagag cccaggctgc gggccgctgc tgcctctcgc catccagctc agccagaccc	1080
ccggcccaaa cagccccatc ttcttgccca ctgatgacaa gtgggactgg ttgctggcca	1140
agacctgggt gcgcaatgcc gagttctcct tccatgaggc cctcacgcac ctgctgcact	1200
cacatctgct gcctgaggtc ttcaccctgg ctaccctgcg tcagctgccc cactgccacc	1260
ctctcttcaa gctgctgac ccgcacaccc gatacacct gcacatcaac aactcgccc	1320
gggagctgct tatcgtgcc a gggcaggtgg tggacaggtc cacaggcatc ggcattgaag	1380
gcttctctga gttgatacag aggaacatga agcagctgaa ctattctctc ctgtgtctgc	1440
ctgaggatat ccggaccoga ggagttgaag acatcccagg ctactactac cgtgatgatg	1500
ggatgcagat ttggggtgca gtggaacgct ttgtctctga aatcatcggt atctactacc	1560
caagtgatga gtctgtccaa gatgacagag agctccaggc ctgggtcaga gagatcttct	1620
ccaagggctt cctaaaccag gagagctcag gtatcccttc ctactggag acccggaag	1680
ccctgggtgca gtatgtcacc atggtgatat tcacctgctc agccaagcat gcggctgtca	1740
gtgcagggca gtttgactcc tgtgcttgga tgcccaacct gccaccacgc atgcagctgc	1800
caccaccac ctccaaaggc ctggcaacat gcgagggctt catagccacc ctcccacctg	1860
tcaatgccac atgtgatgtc atccttgctc tctggttgct gagcaaggag cctggagacc	1920
aaaggcccct gggcacctat ccggatgagc acttcacaga ggaggcccct cggcggagca	1980
tcgccacctt ccagagccgc ctggcccaga tctcgagggg catccaggag cggaaccggg	2040
gcctggtgct gccctacacc tacctagacc ctcccctcat cgagaacagc gtctccatct	2100
aaatcccagg ggaacacagg cccagatgac atocctttga ccacatcgct ctaggataac	2160
tggcaccag agaaaaggac tcctcagaaa aaacaggccc ccatgtgcct ctccctgggac	2220
aaccagactc tgtaactcac cccaccacc atacacacac aaaaaaacag aaacaaaatc	2280
aaaacagaga aagcagaaaa tctaccaaga acagagtctc aggacagAAC cactgagtct	2340
tttgagggt ccaagcctca aagtgccgc agagcccacc ttgagggttt tgctagttgg	2400
ttttgttttg cgtttacagc cgtgggggga agcacataat cccgccccag ggcccactag	2460

- 46 -

catccactga ttggacctta tggtcaccca actcaaggac agccaccaag aagtggctgc 2520
caaagagact gggcgagctg gctcatgccc ataatcccag cactttggga gatggaggcg 2580
ggaaaatcat ttgaggctcag aagttcaagg ccagcctgga cgacatagcg agactccacc 2640
tctaccaaaa aataaaaatt aaaaaacaaa aaaaaaaaaa aaaaa 2685

<210> 29

<211> 2621

<212> DNA

<213> Homo sapiens

<400> 29

gcggagcgct ggggccaca tcacgcctt ggagagcatt gcattggttca ctgtctttta 60
ctttggcaat ggcctggattc ctaccctcat cacggccttt gtccttgcta cctctcaggc 120
ccaagctgga tggctgcaac atgattatgg ccacctgtct gtctacagaa aaccaagtgc 180
gaaccacctt gtccacaaat tcgtcattgg ccacttaaag ggtgcctctg ccaactgggtg 240
gaatcatcgc cacttcacgc accacgcca gcctaacatc ttccacaagg atcccgatgt 300
gaacatgctg cacgtgtttg ttctgggcca atggcagccc atcgagtacg gcaagaagaa 360
gctgaaatac ctgccctaca atcaccagca cgaatacttc ttcttgattg ggccgcccgt 420
gctcatcccc atgtatttcc agtaccagat catcatgacc atgatcgtcc ataagaactg 480
ggtggacctg gcctgggccc tcagctacta catccggttc ttcattcacct acatcccttt 540
ctacggcatc ctgggagccc tccttttctt caacttcac aggttccttg agagccactg 600
gtttgtgtgg gtcacacaga tgaatcacat cgtcatggag attgaccagg aggcctaccg 660
tgactggttc agtagccagc tgacagccac ctgcaacgtg gagcagtcct tcttcaacga 720
ctggttcagt ggacacctta acttcagat tgagcaccac ctcttcccca ccatgccccg 780
gcacaactta cacaagatcg ccccgctggt gaagtctcta tgtgccaage atggcattga 840
ataccaggag aagccgctac tgagggccct gctggacatc atcagggacc tgatgaagtc 900
tggaagctg tggctggacg cctaccttca caaatgaagc cacagcccc gggaacccgt 960
ggggaagggg tgcaggtggg gtgatggcca gaggaatgat gggcttttgt tctgaggggt 1020
gtccgagagg ctggtgtatg cactgctcac ggaccccatg ttggatcttt ctccctttct 1080
cctctccttt ttctcttcac atctcccca tagcaccctg ccctcatggg acctgccctc 1140
cctcagccgt cagccatcag ccatggccct ccagtgctt cctagccct tcttccaagg 1200

- 47 -

agcagagagg tggccaccgg ggggtggctct gtcctacctc cactctctgc ccctaaagat 1260
gggaggagac cagcgggtcca tgggtctggc ctgtgagtct ccccttgacag cctggtcact 1320
aggcatcacc cccgcttttg ttcttcagat gctcttgggg ttcataagggg caggtcctag 1380
tcgggcaggg cccctgaccc tcccggcctg gcttcactct ccctgacggc tgccattggt 1440
ccaccctttc atagagaggg ctgctttgtt acaaagctcg ggtctccctc ctgcagctcg 1500
gttaagtacc cgaggcctct cttaagatgt ccaggggccc aggcccgcg gcacagccag 1560
cccaaaccctt gggccctgga agagtcctcc accccatcac tagagtgtc tgaccctggg 1620
ctttcacggg ccccatcca ccgcctccc aacttgagcc tgtgacctg ggaccaagg 1680
gggagtccct cgtctcttgt gactcagcag aggcagtggc cacgttcagg gaggggccc 1740
ctggcctgga ggctcagccc accctccagc ttttccctcag ggtgtcctga ggtccaagat 1800
tctggagcaa totgaccctt ctccaaaggc tctgttatca gctgggcagt gccagccaat 1860
ccctggccat ttggccccag gggacgtggg ccctgcaggc tgcaggaggg cactggagct 1920
gggaggtctc gtcccagccc tcccctctc ggggctgctg tgtggacggc gctgcctcag 1980
gcactctcct gtctgaacct gcccttactg tgtttaacct gttgctccag gatgcattct 2040
gataggaggg ggcggcaggg ctgggccttg tgacaatctg cctttcacca catggccttg 2100
cctcggtggc cctgactgtc agggagggcc agggaggcag agcgggaggg agtctcagga 2160
ggaggctgcc ctgaggggct ggggaggggg tacctcatga ggaccagggt ggagctgaga 2220
agaggaggag gtgggggctg gaggtgctgg tagctgaggg gacgggcaag tgagagggga 2280
gggaggggaag tcctgggagg atcctgagct gctgttgacg tctaaccac taatcagttc 2340
ttagattcag gggaagggca ggcaccaaca actcagaatg ggggctttcg gggagggcgc 2400
ctagtccccc cagctctaag cagccaggag ggacctgcat ctaagcatct gggttgccat 2460
ggcaatggca tgccccccag ctactgtatg ccccgaccc ccgcagaggc agaatgaacc 2520
catagggagc tgatcgtaat gtttatcatg ttacttcccc accctacat tttttgaaat 2580
aaaataagga attttaaaaa aaaaaaaaaa aagggcggcc g 2621

<210> 30

<211> 2153

<212> DNA

<213> Homo sapiens

- 48 -

<400> 30

tgggtaggag ccagtcattt ccatccatcc acagccatga atttcctccg gcgacgtctc	60
tctgacagca gcttcatggc caacctgcct aatggctata tgacggacct gcaacgcccc	120
gatagctcca ccagctcacc tgcttcccc gccatggaga ggaggcacc ccagcccctg	180
gctgectcct tctcctctcc aggatccagc ctttttagct ccctctccag tgccatgaag	240
caggccccctc aggccacctc aggactgatg gagcctccag gtccctccac gccattgtt	300
caaagaccca ggatcctgtt ggtgatcgat gatgccata cagactggtc gaagtatttc	360
catgggaaga aggtgaatgg agagattgag atccgagtgg agcaggctga attctcagag	420
ttgaacctag ctgcctatgt gaccgggggc tgcattggtg acatgcaggt cgtgagaaat	480
gggaccaaag tggtagagcag atccttcaag ccagacttca tcttgggtccg ccagcatgcc	540
tacagcatgg ccctggggga agactaccgc agcctgggtc tccgctgca gtatggaggg	600
ctgctgctg tcaactctct ctactccgtc tacaacttct gcagcaagcc ctgggtgttc	660
tctcagctca ttaagatctt ccattccctg ggtcctgaga agttcccgt tgtggagcaa	720
acatttttcc ccaaccataa gccaatggtc acagccccac acttcccgtt ggtagtcaag	780
ctgggacatg cccacgctgg aatgggaaag atcaaagtgg aaaaccagct tgacttccag	840
gacatcacca gcgtgggtcgc catggccaaa acatacgcca ccaccgaggc gttcatcgac	900
tccaagtacg acatccgcat ccagaaaatt ggatccaact acaaggctta catgagaacc	960
tccatctctg ggaactggaa ggccaacaca ggctctgcca tgctggagca ggtggccatg	1020
acagagaggt acaggctgtg ggtggacagc tgctcggaaa tgtttggcgg cctggacatc	1080
tgtgccgtca aggctgtcca cagcaaggat ggcagagatt acatcatcga ggtaatggac	1140
agctcaatgc cgctgattgg agagcatgtg gaagaggaca gacagctgat ggccgacctt	1200
gttgtctcca aaatgagcca gctcccgatg ccaggaggca cagcgccctc cccctcaga	1260
ccttgggctc cacagattaa atcagcgaaa tccccagggc aagcccagct ggggcctcag	1320
ctaggccagc cccagccacg ccacctccg caaggaggcc ctcgccaagc tcagtctcct	1380
cagccccaga gatctggaag cccctcccaa cagaggctct cccacaagg ccagcagccc	1440
ctgagcccc agtccggatc tccacagcag caaaggtcac caggctctcc gcagctatcc	1500
cgggcatcca gtggcagctc cccaaaccag gcctccaagc cagggtgccac cctcgcctca	1560
cagccccggc ccctgtgca gggccgtagt acctcccagc aggggtgaaga gtccaagaag	1620
ccagcaccac cccatccgca tctcaacaaa tctcagtccc tgactaacag cctcagcaca	1680

- 49 -

tccgacacct	cccagcgtgg	gaccccaagt	gaagacgagg	ccaaggctga	aaccatccgc	1740
aacctgagga	agtcttttgc	cagcctgttc	tctgactaac	gccatccagg	ctgggagggg	1800
aagagtgcta	tggtaactc	gtccccctcc	tgcctcatct	tccttctcag	ccttggttcc	1860
tgatgggaac	agaatggagg	gcctgagaac	atactttcta	aatgcctttg	accaggaac	1920
cgattatcta	tatttggtcc	cattttcctt	caccgtgaca	ttccagcatt	gtctgactgt	1980
gaggtgggcc	tttgagagcc	tccaggttcc	tcaaaacagg	cctgagcgat	gggcatcaca	2040
ccctctgcct	accacgtgc	atgcttacct	gccagataac	caagtgagat	gtctgcgagt	2100
ggctagtttt	cacattctta	ctagtgtttg	gctcaccttt	gggcaaaggc	ccc	2153

<210> 31

<211> 1470

<212> DNA

<213> Homo sapiens

<400> 31

gacggtcacc	cggtgccagc	tctagccttt	aaattcccgg	ctcggggacc	tccacgcacc	60
gcggctagcg	ccgacaacca	gctagcgtgc	aaggcgccgc	ggctcagcgc	gtaccggcgg	120
gtttcgaaac	cgcagtcctc	cggcgacccc	gaactccgct	cggagcctc	agccccctgg	180
aaagtgatcc	cggcatcgga	gagccaagat	gccggcccac	ttgctgcagg	acgatatctc	240
tagctcctat	accaccacca	ccaccattac	agcgctcct	ccaggggtcc	tgcagaatgg	300
aggagataag	ttggagacga	tgccccctta	cttggaagac	gacattcgcc	ctgatataaa	360
agatgatata	tatgacccca	cctacaagga	taaggaaggc	ccaagcccca	aggttgaata	420
tgtctggaga	aacatcatcc	ttatgtctct	gctacacttg	ggagccctgt	atgggatcac	480
tttgattcct	acctgcaagt	tctacacctg	gctttggggg	gtattctact	attttgtcag	540
tgccctgggc	ataacagcag	gagctcatcg	tctgtggagc	caccgctctt	acaaagctcg	600
gctgccccta	cggctctttc	tgatcattgc	caacacaatg	gcattccaga	atgatgtcta	660
tgaatgggct	cgtgaccacc	gtgcccacca	caagttttca	gaaacacatg	ctgatcctca	720
taattcccga	cgtggctttt	tcttctctca	cgtgggttgg	ctgcttggtc	gcaaacaccc	780
agctgtcaaa	gagaagggga	gtacgctaga	cttgtctgac	ctagaagctg	agaaactggc	840
gatgttccag	aggaggtact	acaaacctgg	cttgctgatg	atgtgcttca	tcctgcccac	900
gcttgtgccc	tggtatttct	ggggtgaaac	ttttcaaaac	agtgtgttcg	ttgccacttt	960

- 50 -

cttgcgatat gctgtggtgc ttaatgccac ctggctggtg aacagtgctg cccacctett	1020
cggatatcgt ccttatgaca agaacattag cccccgggag aatatcctgg tttcacttgg	1080
agctgtgggt gagggcttcc acaactacca ccactccttt ccctatgact actctgccag	1140
tgagtaccgc tggcacatca acttcaacac attcttcatt gattggatgg ccgccctcgg	1200
tctgacctat gaccggaaga aagtctccaa ggccgccatc ttggccagga ttaaaagaac	1260
cggagatgga aactacaaga gtggctgagt ttgggggtccc tcaggttcct ttttcaaaaa	1320
ccagccaggc agaggtttta atgtctgttt attactact gaataatgct accaggatgc	1380
taaagatgat gatgttaacc cattccagta cagtattctt ttaaattca aaagtattga	1440
aagccaaaaa aaaaaaaaaa aaaaaaaaaa	1470

<210> 32

<211> 1245

<212> DNA

<213> Homo sapiens

<400> 32

ggggagagtc tcgccagcc agtcccaggc tgagttcacc tctcacttcc tccagccacc	60
ctgcgtctcg tctcagcctg ggactggctg ggcgagactc tccacctgct ccctgggacc	120
atcgcccacc atggctgtgg cccagcagct gcggggccgag agtgactttg aacagcttcc	180
ggatgatggt gccatctcgg ccaacattgc tgacatcgag gagaagagag gcttcaccag	240
ccactttggt ttcgtcatcg aggtgaagac aaaaggagga tccaagtacc tcatctaccg	300
ccgtaccgc cagttccatg ctttgcagag caagctggag gagcgcttcg ggccagacag	360
caagagcagt gccctggcct gtaccctgcc cacactccca gccaaagtct acgtgggtgt	420
gaaacaggag atcgccgaga tgcggatacc tgccctcaac gcctacatga agagcctgct	480
cagcctgccg gtctgggtgc tgatggatga ggacgtccgg atcttctttt accagtcgcc	540
ctatgactca gagcaggtgc cccaggccat ccgccggctc cgcccgcgca cccggaaagt	600
caagagcgtg tccccacagg gcaacagcgt tgaccgcatg gcagctccga gagcagaggc	660
tctatttgac ttcactggaa acagcaaact ggagctgaat ttcaaagctg gagatgtgat	720
cttcctcctc agtcggatca acaaagactg gctggagggc actgtccggg gagccacggg	780
catcttcctt ctctccttcg tgaagatcct caaagacttc cctgaggagg acgacccac	840

- 51 -

caactggctg cgttgetact actacgaaga caccatcage accatcaagg acatcgcggt 900
ggaggaagat ctcagcagca ctccccctatt gaaagacctg ctggagctca caaggcggga 960
gttccagaga gaggacatag ctctgaatta ccgggacgct gagggggatc tggttcggct 1020
gctgtcggat gaggacgtag cgctcatggt gcggcaggct cgtggcctcc cctcccagaa 1080
gcgcctcttc ccctggaagc tgcacatcac gcagaaggac aactacaggg tctacaacac 1140
gatgccatga gctgacgggtg tccctggagc agtgagggga caccagcaaa aaccttcagc 1200
tctcagagga gattgggacc aggaaaacct gggaggatgg gcaga 1245

<210> 33

<211> 1204

<212> DNA

<213> Homo sapiens

<400> 33

ctctgaggag aagcagcagc aaacatttgc tagtcagaca agtgacaggg aatggattcc 60
aaacagcagt gtgtaaagct aaatgatggc cacttcatgc ctgtattggg atttggcacc 120
tatgcacctc cagaggttcc gagaagtaaa gctttggagg tcacaaaatt agcaatagaa 180
gctgggttcc gccatataga ttctgctcat ttatacaata atgaggagca ggttggactg 240
gccatccgaa gcaagattgc agatggcagt gtgaagagag aagacatatt ctacacttca 300
aagctttggt ccacttttca tcgaccagag ttggtccgac cagccttgga aaactcactg 360
aaaaaagctc aattggacta tgttgacctc tatcttattc attctccaat gtctctaaag 420
ccagggtgagg aactttcacc aacagatgaa aatggaaaag taatatttga catagtggat 480
ctctgtacca cctgggaggc catggagaag tgtaaggatg caggattggc caagtccatt 540
ggggtgtcaa acttcaaccg caggcagctg gagatgatcc tcaacaagcc aggactcaag 600
tacaagcctg tctgcaacca ggtagaatgt catecgtatt tcaaccggag taaattgcta 660
gatttctgca agtcgaaaga tattgttctg gttgcctata gtgctctggg atctcaacga 720
gacaaacgat ggggtggacc gaactccccg gtgctcttgg aggaccagc cctttgtgcc 780
ttggcaaaaa agcacaagcg aaccccagcc ctgattgccc tgcgctacca gctgcagcgt 840
ggggttgtgg tcctggccaa gagctacaat gagcagcgca tcagacagaa cgtgcagggt 900
tttgagttcc agttgactgc agaggacatg aaagccatag atggcctaga cagaaatctc 960
cactatttta acagtgatag ttttgctagc caccctaatt atccatattc agatgaatat 1020

- 52 -

taacatggag agctttgcct gatgtctacc agaagccctg tgtgtggatg gtgacgcaga 1080
 ggacgtctct atgccggtga ctggacatat cacctctact taaatccgtc ctgttttagcg 1140
 acttcagtca actacagctg agtccatagg ccagaaagac aataaatttt tatcattttg 1200
 aaat 1204

<210> 34

<211> 2144

<212> DNA

<213> Homo sapiens

<400> 34

cgggagcgaa agtgcgctga gctgcagtggt ctggtcgaga gtaccccgtagg gagcgtagcg 60
 ccgcggaggg agccgtcccg gcgtaggtgg cgtggccgac cggaccccca actggcgctt 120
 ctccccgcgc ggggtccoga gctaggagat gggaggcaca gctcgtgggc ctgggcggaa 180
 ggatgcgggg ccgcctgggg ccgggctccc gcccagcag cggaggttgg gggatggtgt 240
 ctatgacacc ttcatgatga tagatgaaac caaatgtccc ccctgttcaa atgtactctg 300
 caatccttct gaaccacctc caccagaag actaaatatg accactgagc agtttacagg 360
 agatcatact cagcactttt tggatggagg tgagatgaag gtagaacagc tgtttcaaga 420
 atttggaac agaaaatcca atactattca gtcagatggc atcagtgact ctgaaaaatg 480
 ctctcctact gtttctcagg gtaaaagttc agattgcttg aatacagtaa aatccaacag 540
 ttcatccaag gcacccaaag tgggtgcctct gactccagaa caagccctga agcaatataa 600
 acaccacctc actgcctatg agaaactgga aataattaat tatccagaaa ttacttttgt 660
 aggtccaaat gccaaagaaa gacatggagt tattggtggc cccaataatg gagggtagga 720
 tgatgcagat ggggcctata ttcatgtacc tcgagaccat ctagcttata gatatgaggt 780
 gctgaaaatt attggcaagg ggagtttttg gcaggtggcc aggggtctatg atcacaaact 840
 tcgacagtac gtggccctaa aaatggtgag caatgagaag cgctttcctc gtcaagcagc 900
 tgaggagatc cggattttgg agcatcttaa gaaacaggat aaaactggta gtatgaacgt 960
 tatccacatg ctggaaagtt tcacattccg gaaccatggt tgcattggct ttgaattgct 1020
 gagcatagac ctttatgagc tgattaaaaa aaataagttt cagggtttta gcgtccagtt 1080
 ggtaogcaag tttgccagc ccatcttgca atctttggat gccctccaca aaaataagat 1140

- 53 -

tattcactgc gatctgaagc cagaaaacat tctcctgaaa caccacgggc gcagttcaac 1200
caaggtcatt gactttgggt ccagctgttt cgagtaccag aagctctaca catatatcca 1260
gtctcgggttc tacagagctc cagaaatcat cttaggaagc cgctacagca caccaattga 1320
catatggagt ttctcgtgca tccttgacaga acttttaaca ggacagcctc tcttccctgg 1380
agaggatgaa ggagaccagt tggcctgcat gatggagctt ctagggatgc caccaccaa 1440
acttctggag caatccaaac gtgccaaagta ctttattaat tccaagggca taccctcgta 1500
ctgctctgtg actaccagc cagatgggag ggttggtgctt gtgggggggc gctcacgtag 1560
gggtaaaaag cgggggtccc caggcagcaa agactggggg acagcactga aagggtgtga 1620
tgactacttg tttatagagt tcttgaaaag gtgtcttcac tgggacctt ctgcccgtt 1680
gacctcagct caagcattaa gacaccttg gattagcaag tctgtccca gacctctcac 1740
caccatagac aagggtgtcag ggaaacgggt agttaatcct gcaagtgtt tccagggtt 1800
gggttctaag ctgcctccag ttgttggaat agccaataag cttaaagcta acttaatgtc 1860
agaaaccaat ggtagtatac ccctatgcag tgtattgcca aaactgatta gctagtggac 1920
agagatatgc ccagagatgc atatgtgtat atttttatga tcttacaac ctgcaaattg 1980
aaaaaatgca agccattgg tggatgtttt tgtagagta gactttttt aaacaagaca 2040
aaacattttt atatgattat aaaagaattc ttcaagggt aattacctaa ccagcttgta 2100
ttggccatct ggaatatgca ttaaatgact ttttataggt caaa 2144

<210> 35

<211> 1838

<212> DNA

<213> Homo sapiens

<400> 35

gcacgagcgc agccgccacg ccggggccgc cgagatcggg tgcccgggat gagcctcacc 60
cggaaaaagg gcttctacaa gcaggagctc aacaagaccg cctgggagct gcccaagacc 120
tacgtctccc cgacgcacgt cggcagcggg gcctatggct cctgggtgctc ggccatcgac 180
aagcggtcag gggagaagggt ggccatcaag aagctgagcc gacctttca gtccgagatt 240
ttcgccaagc gcgcctaccg ggagctgctg ctgctgaagc acatgcagca tgagaacgtc 300
attgggctcc tggatgtttt caccacagcc tcctccctgc gcaacttcta tgactctac 360
ctgggtgatgc ccttcatgca gacggatctg cagaagatca tggggatgga gttcagtgag 420

- 54 -

gagaagatcc agtacctggt gtatcagatg ctcaaaggcc ttaagtacat ccactctgct	480
ggggtcgtgc acagggacct gaagccaggc aacctggctg tgaatgagga ctgtgaactg	540
aagattcttg attttgggct ggcgcgacat gcagacgccg agatgactgg ctacgtggtg	600
acccgctggt accgagcccc cgaggatgat ctcagctgga tgcactacaa ccagacagtg	660
gacatctggt ctgtgggctg tatcatggca gagatgctga cagggaaaac tctgttcaag	720
gggaaagatt acctggacca gctgacctag atcctgaaag tgaccggggg gcctggcacg	780
gagtttgtgc agaagctgaa cgacaaagcg gccaaatcct acatccagtc cctgccacag	840
acccccagga aggatttcac tcagctgttc ccacgggcca gccccaggc tgcggacctg	900
ctggagaaga tgctggagct agacgtggac aagcgctga cggccgcgca ggccctcacc	960
catcccttct ttgaaccctt ccgggacctt gaggaagaga cggaggccca gcagccgttt	1020
gatgattcct tagaacacga gaaactcaca gtggatgaat ggaagcagca catctacaag	1080
gagattgtga acttcagccc cattgcccgg aaggactcac ggcgcgggag tggcatgaag	1140
ctgtagggac tcattcttgc tggcaccgcc ggccagacac tgcccaagga ccagtatttg	1200
tcactaccaa actcagccct tcttgggaata cagcctttca agcagaggac agaagggtcc	1260
ttctccttat gtgggaaatg ggccatagtag atgcagaatt caaagatgtc ggttgggaga	1320
aactagctct gatcctaaca ggccacgtta aactgcccat ctggagaatc gcctgcaggt	1380
ggggcccttt ccttcccgcc agagtggggc tgagtgggcg ctgagccagg ccgggggcct	1440
atggcagtga tgctgtgttg gtttcctagg gatgctctaa cgaattacca caaacctggt	1500
ggattgaaac agcagaactt gattccctta cagttctgga ggctggaaat ytgggatgga	1560
ggtgttggca gggctgtggt ccctttgaag gctctgggga agaatccttc cttggctctt	1620
tttagcttgt ggcggcagtg ggcagtcctg ggcattcccc agcttattgc tgcactactc	1680
cagtctctgt ctcttctggt ctctcctctt ttaacaacag tcattggatt tagggccac	1740
cctaatectg tgtgatytta tyttgatect tattaattaa acctgcaaat actctagttc	1800
caaataaagt cacattctca ggttcaggt ggacatga	1838

- 55 -

<210> 36

<211> 1866

<212> DNA

<213> Homo sapiens

<400> 36

cggttcctcgg	cgccgcccggg	gccccagagg	gcagcggcag	caacagcagc	agcagcagca	60
gcgggagtg	agatggcggc	ggcgggcggt	cagggggg	ggggcgggga	gccccgtaga	120
accgagggg	tcggcccggg	ggtcccgggg	gaggtggaga	tggtgaagg	gcagccgttc	180
gacgtggg	cgcgctacac	gcagttgcag	tacatcggcg	agggcgcgta	cggcatggtc	240
agctcggcct	atgaccaagt	gcgcaagact	cgcgtggcca	tcaagaagat	cagccccttc	300
gaacatcaga	cctactgcca	gcgcacgctc	cgggagatcc	agatcctgct	gcgcttcgcg	360
catgagaatg	tcateggcat	ccgagacatt	ctgcggggcg	ccaccctgga	agccatgaga	420
gatgtctaca	ttgtgcagga	cctgatggag	actgaacctg	acaagttgct	gaaaagccag	480
cagctgagca	atgaccatat	ctgctacttc	ctctaccaga	tcctgcgggg	cctcaagtac	540
atccactccg	ccaacgtgct	ccaccgagat	ctaaagccct	ccaacctgct	cagcaacacc	600
acctgcgacc	ttaagatttg	tgatttcggc	ctggcccggg	ttgccgatcc	tgagcatgac	660
cacaccgggt	tcctgacgga	gtatgtgggt	acgcgctggg	accgggcccc	agagatcatg	720
ctgaactcca	agggtatac	caagtccatc	gacatctggg	ctgtgggctg	cattctgggt	780
gagatgctct	ctaaccggcc	catcttcctt	ggcaagcact	acctggatca	gctcaaccac	840
attctgggca	tcctggggctc	cccatcccag	gaggacctga	attgtatcat	caacatgaag	900
gcccgaact	acctacagtc	tctgccctcc	aagaccaagg	tggtttgggc	caagcttttc	960
cccaagtcag	actcaaagc	ccttgacctg	ctggaccgga	tgttaacctt	taaccccaat	1020
aaacggatca	cagtggagga	agcgtgggt	caccctacc	tggagcagta	ctatgacctg	1080
acggatgagc	cagtggccga	ggagcccttc	accttcgcca	tggagctgga	tgacctacct	1140
aaggagcggc	tgaaggagct	catcttccag	gagacagcac	gcttccagcc	cggagtgctg	1200
gaggccccct	agcccagaca	gacatctctg	caccctgggg	cctggacctg	cctcctgcct	1260
gcccctctcc	cgccagactg	ttagaaaatg	gacactgtgc	ccagcccggg	ccttggcagc	1320
ccaggccggg	gtggagcatg	ggcctggcca	cctctctcct	ttgctgaggc	ctccagcttc	1380
aggcaggcca	aggccttctc	ctccccaccc	gccctcccca	cggggcctcg	ggagctcagg	1440

- 56 -

```

tggccccagt tcaatctccc gctgctgctg ctgctgcgcc cttaccttcc ccagcgtccc 1500
agtctctggc agttctggaa tggaagggtt ctggctgccc caacctgctg aagggcagag 1560
gtggaggggtg gggggcgctg agtagggact cagggccatg cctgcccccc tcatctcatt 1620
caaaccccac cctagtttcc ctgaagggaac attccttagt ctcaagggtt agcatccctg 1680
aggagccagg ccggggccgaa tcccctccct gtcaaagctg tcaacttcgcg tgccctcgct 1740
gcttctgtgt gtggtgagca gaagtggagc tggggggcgt ggagagcccc gcgcccctgc 1800
cacctccctg acccgtctaa tatataaata tagagatgtg tctatggctg aaaaaaaaaa 1860
aaaaaa 1866

```

<210> 37

<211> 3078

<212> DNA

<213> Homo sapiens

<400> 37

```

catggagccc ttgaagagcc tcttcctcaa gagccctcta gggatcatgga atggcagtgg 60
cagcgggggt ggtgggggag gtggaggagg ccggcctgag gggatctcaa aggcagcggg 120
ttatgccaac ccggtgtgga cagccctgtt cgactacgag cccagtgggc aggatgagct 180
ggccctgagg aagggtgacc gtgtggaggt gctgtcccgg gacgcagcca tctcaggaga 240
cgagggtctg tgggcgggac aggtgggtgg ccagggtggc atcttcccgt ccaactatgt 300
gtctcgggggt ggcggcccg cccctgcga ggtggccagc ttccaggagc tgcggctgga 360
ggaggtgatc ggcattggag gctttggcaa ggtgtacagg ggcagctggc gaggtgagct 420
ggtggctgtg aaggcagctc gccaggaccc cgatgaggac atcagtgtga cagccgagag 480
cgttcgccag gagggccggc tcttcgcat gctggcacac cccaacatca ttgccctcaa 540
ggctgtgtgc ctggaggagc ccaacctgtg cctgggtgatg gagtatgcag ccggtgggac 600
cctcagccga gctctggcag ggcggcgctg gctcccccatt gtgctggtca actgggctgt 660
gcagattgcc cgtgggatgc actacctgca ctgcgaggcc ctggtgcccg tcatccaccg 720
tgatctcaag tccaacaaca ttttgctgct gcagccatt gagagtgcag acatggagca 780
caagaccctg aagatcaccg actttggcct ggcccgagag tggcacaaaa ccacacaaat 840
gagtgcgcgc ggcacctacg cctggatggc tcctgaggtt atcaaggcct ccacctctc 900
taagggcagt gacgtctgga gttttgggggt gctgctgtgg gaactgctga ccggggaggt 960

```


- 57 -

gccataccgt ggcattgact gccttgctgt ggcctatggc gtagctgtta acaagctcac 1020
actgcccata ccatccacct gcccagagcc cttcgcacag cttatggccg actgctgggc 1080
gcaggacccc cacgcagggc cggacttcgc ctccatcctg cagcagttgg aggcgctgga 1140
ggcacaggtc ctacgggaaa tgccgcggga ctcccttccat tccatgcagg aaggctggaa 1200
gcgcgagatc caggggtctct tcgacgagct gcgagccaag gaaaaggaaac tactgagccg 1260
cgaggaggag ctgacgcgag cggcgcgcgga gcagcgggtca caggcggagc agctgcggcg 1320
gcgcgagcac ctgctggccc agtgggagct agagggtgttc gagcgcgagc tgacgctgct 1380
gctgcagcag gtggaccgcg agcgaccgca cgtgcgccgc cgccgcggga cattcaagcg 1440
cagcaagctc cgggcgcgcg acggcgggcg gcgtatcagc atgccactcg acttcaagca 1500
ccgcatcacc gtgcaggcct caccgcgcct tgaccggagg agaaacgtct tcgaggtcgg 1560
gcctggggat tcgcccacct ttccccggtt ccgagccatc cagttggagc ctgcagagcc 1620
aggccaggca tggggccgcc agtccccccg acgtctggag gactcaagca atggagagcg 1680
gcgagcatgc tgggcttggg gtcccagttc cccaagcct ggggaagccc agaattgggag 1740
gagaaggctc cgcattggacg aagccacatg gtacctggat tcagatgact catccccctt 1800
aggatctcct tccacacccc cagcactcaa tggtaacccc ccgcggccta gcctggagcc 1860
cgaggagccc aagaggcctg tccccgcaga gcgcggtagc agctctggga cgcccaagct 1920
gatccagcgg gcgctgctgc gcggcaaccgc cctgctcgcc tcgctggggc ttggccgcga 1980
cctgcagccg ccgggaggcc caggacgcga gcgcggggag tccccgacaa cccccccac 2040
gccaacgccc gcgccttgc cgaccgagcc gccccttcc ccgctcatct gcttctcgt 2100
caagacgccc gactccccgc cactcctgc acccctgttg ctggacctgg gtatccctgt 2160
gggccagcgg tcagccaaga gcccgcgacg tgaggaggag cccgcggag gcactgtctc 2220
acccccaccg gggacatcac gctctgctcc tggcaccoca ggcacccac gttcaccacc 2280
cctgggcctc atcagccgac ctgggcctc gcccttcgc agccgcattg atccctggag 2340
ctttgtgtca gctgggccac ggccttctcc cctgccatca ccacagcctg caccocgcg 2400
agcaccctgg acctgttcc cggactcaga ccccttctgg gactccccac ctgccaaccc 2460
cttccagggg ggccccagc actgcagggc acagaccaa gacatgggtg cccaggcccc 2520
gtgggtgccg gaagcggggc cttgagtggg ccaggccact ccccgagct ccagctgcct 2580
taggaggagt cacagcatac actggaacag gagctgggtc agcctctgca gctgcctcag 2640
tttccccagg gacccacccc ccctttgggg gtcaggaaca ctacactgca caggaagcct 2700

- 58 -

tcacactgga aggggggacct gcgccccac atctgaaacc tgtaggtccc cccagctcac 2760
ctgccctact ggggcccac actgtacca gctggttggg aggaccagag cctgtctcag 2820
ggaattgcct gctggggtga tgcaggagg aggggagggtg cagggaagag gggccggcct 2880
cagctgtcac cagcactttt gaccaagtc tgctactgcg gcccctgcc tagggcttag 2940
agcatggacc tcctgccctg ggggtcatct ggggccaggg ctctctggat gccttcctgc 3000
tgccccagcc agggttggag tcttagcctc gggatccagt gaagccagaa gccaaataaa 3060
ctcaaaagct gtctcccc 3078

<210> 38

<211> 14896

<212> DNA

<213> Homo sapiens

<400> 38

cagcgggtgcg agctccaggc ccatgcactg aggaggcgga aacaagggga gccccagag 60
ctccatcaag ccccctccaa aggctccct acccgggtcca cgcacccac ccccctccc 120
cgcctcctcc caattgtgca tttttgcagc cggaggcggc tccgagatgg ggctgtgagc 180
ttcgcccggg gagggggaaa gagcagcgag gagtgaagcg ggggggtggg gtgaagggtt 240
tggtatttcgg ggcagggggc gcacccccgt cagcaggccc tcccgaagg gctcggaact 300
ctacctcttc acccacgcc ctggtgcgct ttgccgaagg aaagaataag aacagagaag 360
gaggaggggg aaaggaggaa aagggggacc cccaactgg ggggggtgaa ggagagaagt 420
agcaggacca gaggggaagg ggctgctgct tgcatcagcc cacaccatgc tgaccccgcc 480
gttgctcctg ctgctgcccc tgctctcagc tctggtcgag gcggctatcg acgcccctaa 540
gacttgcagc cccaagcagt ttgcctgcag agatcaaata acctgtatct caaagggtg 600
gcggtgcgac ggtgagaggg actgccaga cggatctgac gaggcccctg agatttgtcc 660
acagagtaag gccagcgat gccagccaaa cgagcataac tgcttgggta ctgagctgtg 720
tgttcccatg tcccgctct gcaatggggg ccaggactgc atggacggct cagatgaggg 780
gccccactgc cgagagctcc aaggcaactg ctctcgctg ggctgccagc accatttgtt 840
ccccacactc gatgggcca cctgctactg caacagcagc tttcagcttc aggcagatgg 900
caagacctgc aaagattttg atgagtgtc agtgtacggc acctgcagcc agctatgcac 960
caacacagac ggctccttca tatgtggctg tggtgaagga tacctcctgc agccggataa 1020

- 59 -

ccgctcctgc aaggccaaga acgagccagt agaccggccc cctgtgctgt tgatagccaa 1080
ctcccagaac atcttggcca cgtacctgag tggggcccag gtgtctacca tcacacctac 1140
gagcacgcgg cagaccacag ccatggactt cagctatgcc aacgagaccg tatgctgggt 1200
gcatgttggg gacagtgtgt ctcagacgca gctcaagtgt gcccgcatgc ctggcctaaa 1260
gggcttcgtg gatgagcaca ccatcaacat ctccctcagt ctgcaccacg tggaacagat 1320
ggccatcgac tggctgacag gcaacttcta ctttgtggat gacatcgatg ataggatctt 1380
tgtctgcaac agaaatgggg acacatgtgt cacattgcta gacctggaac tctacaaccc 1440
caagggcatt gccctggacc ctgccatggg gaaggtgttt ttcactgact atgggcagat 1500
cccaaagggtg gaacgctgtg acatggatgg gcagaaccgc accaagctcg tcgacagcaa 1560
gattgtgttt cctcatggca tcacgctgga cctggtcage cgccttgtct actgggcaga 1620
tgcctatctg gactatattg aagtgggtgga ctatgagggc aagggccgcc agaccatcat 1680
ccagggcatc ctgattgagc acctgtacgg cctgactgtg tttgagaatt atctctatgc 1740
caccaactcg gacaatgcca atgcccagca gaagacgagt gtgatccgtg tgaaccgctt 1800
taacagcacc gagtaccagg ttgtcacccg ggtggacaag ggtggtgccc tccacatcta 1860
ccaccagagg cgtcagcccc gagtgaggag ccatgcctgt gaaaacgacc agtatgggaa 1920
gcggggtggc tgetctgaca tctgcctgct ggccaacage cacaaggcgc ggacctgccg 1980
ctgccgttcc ggcttcagcc tgggcagtga cgggaagtca tgcaagaagc cggagcatga 2040
gctgttcctc gtgtatggca agggccggcc aggcattcat cggggcatgg atatgggggc 2100
caaggtcccg gatgagcaca tgatcccat tgaaaacctc atgaaccccc gagccctgga 2160
cttccacgct gagaccggct tcattctactt tgccgacacc accagctacc tcattggccg 2220
ccagaagatt gatggcactg agcgggagac catcctgaag gacggcatcc acaatgtgga 2280
gggtgtggcc gtggactgga tgggagacaa tctgtactgg acggacgatg ggcccaaaaa 2340
gacaatcagc gtggccaggc tggagaaagc tgctcagacc cgcaagactt taatcgaggg 2400
caaaatgaca caccacaggg ctattgtggt ggatccactc aatgggtgga tgtactggac 2460
agactgggag gaggacccca aggacagtcg gcgtgggcgg ctggagaggg cgtggatgga 2520
tggctcacac cgagacatct ttgtcacctc caagacagtg ctttggccca atgggctaag 2580
cctggacatc ccggctgggc gcctctactg ggtggatgcc ttctacgacc gcatcgagac 2640
gatactgctc aatggcacag accggaagat tgtgtatgaa ggtcctgagc tgaaccacgc 2700
ctttggcctg tgtcaccatg gcaactacct cttctggact gagtatcgga gtggcagtgt 2760

- 60 -

ctaccgcttg	gaacggggtg	taggaggcgc	acccccact	gtgacccttc	tgcgcagtga	2820
gcgcccccc	atctttgaga	tccgaatgta	tgatgccag	cagcagcaag	ttggcaccaa	2880
caaatgccgg	gtgaacaatg	gcggctgcag	cagcctgtgc	ttggccaccc	ctgggagccg	2940
ccagtgcgcc	tgtgctgagg	accaggtggt	ggacgcagac	ggcgtcactt	gcttggcgaa	3000
cccatcctac	gtgcctccac	cccagtgcoa	gccaggcgag	tttgccctgtg	ccaacagccg	3060
ctgcatccag	gagcgctgga	agtgtgacgg	agacaacgat	tgcctggaca	acagtgatga	3120
ggccccagcc	ctctgccatc	agcacacctg	cccctcggac	cgattcaagt	gcgagaacaa	3180
ccggtgcac	cccaaccgct	ggetctgcga	cggggacaat	gactgtggga	acagtgaaga	3240
tgagtccaat	gccacttggt	cagcccgcac	ctgccccccc	aaccagttct	cctgtgccag	3300
tggcogctgc	atccccatct	cctggacgtg	tgatctggat	gacgactgtg	gggaccgctc	3360
tgatgagtct	gcttcgtgtg	cctatcccac	ctgcttcccc	ctgactcagt	ttacctgcaa	3420
caatggcaga	tgtatcaaca	tcaactggag	atgcgacaat	gacaatgact	gtggggacaa	3480
cagtgcagaa	gcgggctgca	gccactcctg	ttctagcacc	cagttcaagt	gcaacagcgg	3540
gcgttgcatc	cccagacact	ggacctgcga	tggggacaat	gactgcggag	actacagtga	3600
tgagacacac	gccaactgca	ccaaccaggc	cacgaggccc	cctggtggct	gccacactga	3660
tgagttccag	tgccggctgg	atggactatg	catccccctg	cgggtggcgt	gcgatgggga	3720
cactgactgc	atggactcca	gcgatgagaa	gagctgtgag	ggagtgaccc	acgtctgcga	3780
tcccagtgtc	aagtttggtc	gcaaggactc	agctcgggtg	atcagcaaag	cgtgggtgtg	3840
tgatggcgac	aatgaactgtg	aggataactc	ggacgaggag	aactgcgagt	ccctggcctg	3900
caggccaccc	tgcaccctt	gtgccaacaa	cacctcagtc	tgcctgcccc	ctgacaagct	3960
gtgtgatggc	aacgacgact	gtggcgacgg	ctcagatgag	ggcgagctct	gcgaccagtg	4020
ctctctgaat	aacggtggct	gcagccacaa	ctgctcagtg	gcacctggcg	aaggcattgt	4080
gtgttcctgc	cctctgggca	tggagctggg	gcccgcacaac	cacacctgcc	agatccagag	4140
ctactgtgcc	aagcatctca	aatgcagcca	aaagtgcgac	cagaacaagt	tcagcgtgaa	4200
gtgctcctgc	tacgagggct	gggtcctgga	acctgacggc	gagagctgcc	gcagcctgga	4260
ccccttcaag	ccgttcatca	ttttctccaa	ccgccatgaa	atccggcgca	tcgatcttca	4320
caaaggagac	tacagcgtcc	tggtgcccg	cctgcgcaac	accatcgccc	tggacttcca	4380
cctcagccag	agcgccctct	actggaccga	cgtggtggag	gacaagatct	accgcgggaa	4440
gctgctggac	aacggagccc	tgactagttt	cgaggtgggtg	attcagtatg	gcctggccac	4500
acccgagggc	ctggctgtag	actggattgc	aggcaacatc	tactgggtgg	agagtaacct	4560

- 61 -

ggatcagatc	gaggtggcca	agctggatgg	gacctccgg	accacctgc	tggccggtga	4620
cattgagcac	ccaagggcaa	tgcactgga	tccccgggat	gggatcctgt	tttggacaga	4680
ctgggatgcc	agcctgcccc	gcattgaggc	agcctccatg	agtggggctg	ggcgccgcac	4740
cgtgcaccgg	gagaccggct	ctgggggctg	gccaacggg	ctcaccgtgg	actacctgga	4800
gaagcgcata	ctttggattg	acgccaggtc	agatgccatt	tactcagccc	gttacgacgg	4860
ctctggccac	atggaggtgc	ttcggggaca	cgagttcctg	tgcacccgt	ttgcagtgc	4920
gctgtacggg	ggggaggtct	actggactga	ctggcgaaca	aacacactgg	ctaaggccaa	4980
caagtggacc	ggccacaatg	tcaccgtggt	acagaggacc	aacaccagc	cctttgacct	5040
gcaggtgtac	cacctctccc	gccagcccat	ggctcccaat	ccctgtgagg	ccaatggggg	5100
ccagggcccc	tgctcccacc	tgtgtctcat	caactacaac	cggaccgtgt	cctgcgcctg	5160
ccccacctc	atgaagctcc	acaaggacaa	caccacctgc	tatgagttta	agaagttcct	5220
gctgtacgca	cgtcagatgg	agatccgagg	tgtggacctg	gatgctccct	actacaacta	5280
catcatctcc	ttcacgggtgc	ccgacatcga	caacgtcaca	gtgctagact	acgatgcccg	5340
cgagcagcgt	gtgtactggt	ctgacgtgcg	gacacaggcc	atcaagcggg	ccttcatcaa	5400
cggcacaggc	gtggagacag	togtctctgc	agacttgcca	aatgcccacg	ggctggctgt	5460
ggactgggtc	tcccgaacc	tgttctggac	aagctatgac	accaataaga	agcagatcaa	5520
tgtggcccgg	ctggatggct	ccttcaagaa	cgcagtgggtg	cagggcctgg	agcagcccca	5580
tggccttgte	gtccaccctc	tgcgtgggaa	gctctactgg	accgatgggtg	acaacatcag	5640
catggccaac	atggatggca	gcaatcgcac	cctgctcttc	agtggccaga	agggccccgt	5700
gggcctggct	attgacttcc	ctgaaagcaa	actctactgg	atcagctccg	ggaaccatac	5760
catcaaccgc	tgcaacctgg	atgggagtgg	gctggaggte	atcgatgcca	tgcgagacca	5820
gctgggcaag	gccaccgccc	tggccatcat	gggggacaag	ctgtgggtggg	ctgatcaggt	5880
gtcggaaaag	atgggcacat	gcagcaaggc	tgacggctcg	ggctccgtgg	tccttcggaa	5940
cagcaccacc	ctggtgatgc	acatgaaggt	ctatgacgag	agcatccagc	tggaccataa	6000
gggcaccaac	ccctgcagtg	tcaacaacgg	tgactgctcc	cagctctgcc	tgcccacgtc	6060
agagacgacc	cgctcctgca	tgtgcacagc	cggctatagc	ctccggagtg	gccagcaggc	6120
ctgcgagggc	gtaggttcct	ttctcctgta	ctctgtgcat	gagggaatca	ggggaattcc	6180
cctggatecc	aatgacaagt	cagatgccct	ggtcccagtg	tccgggacct	cgctggctgt	6240
cggcatcgac	ttccacgctg	aaaatgacac	catctactgg	gtggacatgg	gcctgagcac	6300

- 62 -

gatcagccgg gccaaagcggg accagacgtg gcgtgaagac gtggtgacca atggcattgg 6360
ccgtgtggag ggcattgcag tggactggat cgcaggcaac atctactgga cagaccaggg 6420
ctttgatgtc atcgaggtcg cccggctcaa tggtctcttc cgctacgtgg tgatctccca 6480
gggtctagac aagccccggg ccatcacctg ccacccggag aaaggggtact tgttctggac 6540
tgagtggggg cagtatccgc gtattgagcg gtctcggcta gatggcacgg agcgtgtggg 6600
gctgggtcaac gtcagcatca gctggcccaa cggcatctca gtggactacc aggatgggaa 6660
gctgtactgg tgcgatgcac ggacagacaa gattgaacgg atcgacctgg agacaggtga 6720
gaaccgcgag gtggttctgt ccagcaacaa catggacatg ttttcagtgt ctgtgtttga 6780
ggatttcata tactggagtg acaggactca tgccaacggc tctatcaagc gcgggagcaa 6840
agacaatgcc acagactccg tgcccctgcg aaccggcatc ggctccagc ttaaagacat 6900
caaagtcttc aaccgggacc ggcagaaagg caccaacgtg tgcgcggtgg ccaatggcgg 6960
gtgccagcag ctgtgcctgt accggggcgg tgggcagcgg gcctgcgcct gtgccacgg 7020
gatgctggct gaagacggag catcgtgcg cgagtatgcc ggctacctgc tctactcaga 7080
gcgcaccatt ctcaagagta tccacctgtc ggatgagcgc aacctcaatg cgcctgtgca 7140
gcccttcgag gacctgagc acatgaagaa cgtcatcgcc ctggcctttg actaccgggc 7200
aggcacctct ccgggcaccc ccaatcgcat cttcttcagc gacatccact ttgggaacat 7260
ccaacagatc aacgacgatg gctccaggag gatcaccatt gtggaaaacg tgggctccgt 7320
ggaaggcctg gcctatcacc gtggctggga cactctctat tggacaagct acacgacatc 7380
caccatcacg cgccacacag tggaccagac ccgcccaggg gccttcgagc gtgagaccgt 7440
catcactatg tctggagatg accaccacg ggccttcggt ttggacgagt gccagaacct 7500
catgttctgg accaactgga atgagcagca tcccagcatc atgcgggcgg cgctctcggg 7560
agccaatgtc ctgaccctta tcgagaagga catccgtacc cccaatggcc tggccatcga 7620
ccaccgtgcc gagaagetct acttctctga cgccaccctg gacaagatcg agcgggtgcga 7680
gtatgacggc toccaccgct atgtgatcct aaagtcagag cctgtccacc ccttcgggct 7740
ggccgtgtat ggggagcaca ttttctggac tgactgggtg cggcgggcag tgcagcgggc 7800
caacaagcac gtgggcagca acatgaagct gctgcgcgtg gacatcccc agcagcccat 7860
gggcatcacc gccgtggcca acgacaccaa cagctgtgaa ctctctccat gccgaatcaa 7920
caacggtggc tgccaggacc tgtgtctgct cactcaccag ggccatgtca actgctcatg 7980
ccgagggggc cgaatcctcc aggatgacct cacctgccga gcgggtgaatt cctcttgccg 8040
agcacaagat gagtttgagt gtgccaatgg cgagtgcac aacttcagcc tgacctgcga 8100

- 63 -

cggcgtcccc cactgcaagg acaagtccga tgagaagcca tcctactgca actcccgccg 8160
ctgcaagaag actttccggc agtgcagcaa tgggcgctgt gtgtccaaca tgctgtggtg 8220
caacggggcc gacgactgtg gggatggctc tgacgagatc ccttgcaaca agacagcctg 8280
tggtgtgggc gagttccgct gccgggacgg gacctgcac gggaactcca gccgctgcaa 8340
ccagtttgtg gattgtgagg acgcctcaga tgagatgaac tgcagtgcc aagactgcag 8400
cagctacttc cgcctgggag tgaagggcgt gctcttccag ccctgcgagc ggacctcact 8460
ctgctacgca cccagctggg tgtgtgatgg cgccaatgac tgtggggact acagtgatga 8520
gcgcgactgc ccaggtgtga aacgccccag atgcctcttg aattacttcg cctgccctag 8580
tgggcgctgc atcccatga gctggacgtg tgacaaagag gatgactgtg aacatggcga 8640
ggacgagacc cactgcaaca agttctgctc agaggcccag tttgagtgcc agaaccatcg 8700
ctgcatctcc aagcagtggc tgtgtgacgg cagcgatgac tgtggggatg gctcagacga 8760
ggctgctcac tgtgaaggca agacgtgcgg ccctcctcc ttctcctgcc ctggcaccca 8820
cgtgtgcgtc cccgagcgct ggctctgtga cggtgacaaa gactgtgctg atgggtgcaga 8880
cgagagcatc gcagctgggt gcttgtacaa cagcacttgt gacgaccgtg agttcatgtg 8940
ccagaaccgc cagtgcattc ccaagcactt cgtgtgtgac cagcaccgtg actgtgcaga 9000
tggctctgat gagtcccccg agtgtgagta cccgacctgc ggccccagtg agttccgctg 9060
tgccaatggg cgctgtctga gctcccgcca gtgggagtgat gatggcgaga atgactgcca 9120
cgaccagagt gacgaggctc ccaagaacct aactgcacc agcccagagc acaagtgcaa 9180
tgctctgtca cagttcctgt gcagcagtgg gcgctgtgtg gctgaggcac tgctctgcaa 9240
cggccaggat gactgtggcg acagctcgga cgagcgtggc tgccacatca atgagtgtct 9300
cagccgcaag ctgagtggct gcagccagga ctgtgaggac ctcaagatcg gcttcaagtg 9360
ccgctgtcgc cctggcttcc ggctgaagga tgacggccgg acgtgtgctg atgtggacga 9420
gtgcagcacc accttccct gcagccagcg ctgcatcaac acctatggca gctataagtg 9480
tctgtgtgtg gagggctatg caccgccgg cggcgacccc cacagctgca aggctgtgac 9540
tgacgaggaa ccgtttctga tcttcgcca cgggtactac ctgcgcaagc tcaacctgga 9600
cgggtccaac tacacgttac ttaagcagg cctgaacaac gccgttgctt tggattttga 9660
ctaccgagag cagatgatct actggacaga tgtgaccacc cagggcagca tgatccgaag 9720
gatgcacctt aacgggagca atgtgcaggt cctacaccgt acaggcctca gcaaccccga 9780
tgggctggct gtggactggg tgggtggcaa cctgtactgg tgcgacaaag gccgggacac 9840

- 64 -

catcgagggtg tccaagctca atgggggcta tcggacgggtg ctggtcagct ctggcctccg 9900
tgagcccagg gctctggtgg tggatgtgca gaatgggtac ctgtactgga cagactgggg 9960
tgaccattca ctgatcggcc gcatcggcat ggatgggtcc agccgcagcg tcatcgtgga 10020
caccaagatc acatggccca atggcctgac gctggactat gtcactgagc gcatctactg 10080
ggccgacgcc cgcgaggact acattgaatt tgccagcctg gatggctcca atcgccacgt 10140
tgtgctgagc caggacatcc cgcacatctt tgcactgacc ctgtttgagg actacgtcta 10200
ctggaccgac tgggaaacaa agtccattaa ccgagccac aagaccacgg gcaccaacaa 10260
aacgctcctc atcagcacgc tgcaccggcc catggacctg catgtcttcc atgccctgcg 10320
ccagccagac gtgcccaatc acccctgcaa ggtcaacaat ggtggctgca gcaacctgtg 10380
cctgctgtcc cccgggggag ggcacaaatg tgctgcccc accaacttct acctgggcag 10440
cgatgggcgc acctgtgtgt ccaactgcac ggctagccag tttgtatgca agaacgacaa 10500
gtgcatcccc ttctggtgga agtgtgacac cgaggacgac tgcggggacc actcagacga 10560
gcccccgac tgccctgagt tcaagtgcg gcccgacag ttccagtgtt ccacaggtat 10620
ctgcacaaac cctgccttca tctgcgatgg cgacaatgac tgccaggaca acagtgcga 10680
ggccaactgt gacatccacg tctgcttgcc cagtcagttc aaatgcacca acaccaaccg 10740
ctgtattccc ggcattcttc gctgcaatgg gcaggacaac tgcggagatg gggaggatga 10800
gagggactgc cccgaggtga cctgcgcccc caaccagttc cagtgtctca ttaccaaacg 10860
gtgcatcccc cgggtctggg tctgcgaccg ggacaatgac tgtgtggatg gcagtgatga 10920
gcccgccaac tgcacccaga tgacctgtgg tgtggacgag ttccgctgca aggattcggg 10980
ccgctgcate ccagcgcgtt ggaagtgtga cggagaggat gactgtgggg atggctcgga 11040
tgagcccaag gaagagtgtg atgaacgcac ctgtgagcca taccagttcc gctgcaagaa 11100
caaccgctgc gtgcccggcc gctggcagtg cgactacgac aacgattgcg gtgacaactc 11160
cgatgaagag agctgcaccc ctcgccctg ctccgagagt gagttctcct gtgccaacgg 11220
ccgctgcate gcggggcgct ggaaatgcga tggagaccac gactgcgcgg acggctcgga 11280
cgagaaagac tgcaccccc gctgtgacat ggaccagttc cagtgcgaaga gcggccactg 11340
cateccccctg cgctggcgct gtgacgcaga cgcgactgc atggacggca gcgacgagga 11400
ggcctgcggc actggcgctg ggacctgccc cctggacgag ttccagtgc acaacacctt 11460
gtgcaagccg ctggcctgga agtgcgatgg cgaggatgac tgtggggaca actcagatga 11520
gaaccccgag gagtgtgccc ggttcgtgtg ccctcccaac cggcccttcc gttgcaagaa 11580
tgaccgcgtc tgtctgtgga tcgggcgcca atgcgatggc acggacaact gtggggatgg 11640

- 65 -

gactgatgaa gaggactgtg agccccccac agcccacacc acccactgca aagacaagaa 11700
ggagtttctg tgccggaacc agcgctgcct ctccctcctcc ctgcgctgca acatgttcga 11760
tgactgcggg gacggctctg acgaggagga ctgcagcatc gaccccaagc tgaccagctg 11820
cgccaccaat gccagcatct gtgggggacga ggcacgctgc gtgcgcaccg agaaagcggc 11880
ctactgtgcc tgccgctcgg gcttccacac cgtgcccggc cagcccggat gccaagacat 11940
caacgagtgc ctgcgcttcg gcacctgctc ccagctctgc aacaacacca agggcggcca 12000
cctctgcagc tgcgctcggg acttcatgaa gacgcacaac acctgcaagg ccgaaggctc 12060
tgagtaccag gtccctgtaca tcgctgatga caatgagatc cgcagcctgt tccccggcca 12120
ccccattcg gcttacgagc aggcattcca gggtgacgag agtgtccgca ttgatgctat 12180
ggatgtccat gtcaaggctg gccgtgtcta ttggaccaac tggcacacgg gcaccatctc 12240
ctaccgcagc ctgccacctg ctgcgcctcc taccacttcc aaccgccacc ggcgacagat 12300
tgaccggggt gtcaccaccc tcaacatttc agggctgaag atgccagag gcctcgccat 12360
cgactgggtg gccggaaacg tgtactggac cgactcgggc cgagatgtga ttgaggtggc 12420
gcagatgaag ggcgagaacc gcaagacgct catctcgggc atgattgacg agccccacgc 12480
cattgtggtg gaccactga gggggacat gtactggtca gactggggca accaccccaa 12540
gattgagacg gcagcgatgg atgggacgct tcgggagaca ctggtgcagg acaacattca 12600
gtggcccaca ggctggccg tggattatca caatgagcgg ctgtactggg cagacgcaa 12660
gctttcagtc atcggcagca tccggctcaa tggcacggac cccattgtgg ctgctgacag 12720
caaacgaggc ctaagtcacc ccttcagcat cgacgtcttt gaggattaca tctatggtgt 12780
cacctacatc aataatcgtg tcttcaagat ccataagttt ggccacagcc ccttggtcaa 12840
cctgacaggg ggctgagcc acgcctctga cgtggtcctt taccatcagc acaagcagcc 12900
cgaagtgacc aaccatgtg accgcaagaa atgcgagtgg ctctgcctgc tgagccccag 12960
tgggcctgtc tgcacctgtc ccaatgggaa gcggctggac aacggcacat gcgtgcctgt 13020
gcctctcca acgccccccc cagatgctcc ccggcctgga acctgtaacc tgcaagtgtt 13080
caacggtggc agctgtttcc tcaatgcacg gaggcagccc aagtgccgct gccaaacccg 13140
ctacacgggt gacaagtgtg aactggacca gtgctgggag cactgtcgca atgggggcac 13200
ctgtgctgcc tccccctctg gcatgcccac gtgccggtgc cccacgggct tcacgggccc 13260
caaatgcacc cagcaggtgt gtgcgggcta ctgtgccaac aacagcacct gcactgtcaa 13320
ccagggaac cagccccagt gccgatgcct acccggttc ctgggcgacc gctgccagta 13380

- 66 -

ccggcagtgc tctggctact gtgagaactt tggcacatgc cagatggctg ctgatggctc 13440
ccgacaatgc cgctgcactg cctactttga gggatcgagg tgtgaggtga acaagtgcag 13500
ccgctgtctc gaaggggcct gtgtggtcaa caagcagagt ggggatgtca cctgcaactg 13560
cacggatggc cgggtggccc ccagctgtct gacctgcgtc ggccactgca gcaatggcgg 13620
ctcctgtacc atgaacagca aatgatgcc tgagtgccag tgcccacccc acatgacagg 13680
gccccggtgt gaggagcacg tcttcagcca gcagcagcca ggacatatag cctccatcct 13740
aatccctctg ctgttgctgc tgetgctggt tctggtggcc ggagtgggtat tctggtataa 13800
gcggcgagtc caaggggcta agggcttcca gcaccaacgg atgaccaacg gggccatgaa 13860
cgtggagatt ggaaacccca cctacaagat gtacgaaggc ggagagcctg atgatgtggg 13920
aggcctactg gacgctgact ttgccctgga ccctgacaag cccaccaact tcaccaaccc 13980
cgtgtatgcc acactctaca tggggggcca tggcagtcgc cactccctgg ccagcacgga 14040
cgagaagcga gaactcctgg gccggggccc tgaggacgag ataggggacc ccttggcata 14100
gggccctgcc ccgtcggact gccccagaa agcctcctgc cccctgccgg tgaagtcctt 14160
cagtgagccc ctccccagcc agcccttccc tggccccgcc ggatgtataa atgtaaaaat 14220
gaaggaatta catTTTTatT gtgagcgagc aagccggcaa gcgagcacag tattatttct 14280
ccatccccctc cctgcctget ccttggcacc cccatgctgc cttcagggag acaggcaggg 14340
agggcttggg gctgcacctc ctaccctccc accagaacgc accccactgg gagagctggt 14400
ggtgcagcct tcccctccct gtataagaca ctttgccaag gctctcccct ctgccccat 14460
ccctgcttgc ccgtccccc acgttcctga gggctaattc tgggaaggga gagttctttg 14520
ctgcccctgt ctggaagacg tggctctggg tgaggtaggc gggaaaggat ggagtgtttt 14580
agttcttggg ggaggccacc ccaaacccca gcccacactc caggggcacc tatgagatgg 14640
ccatgetcaa cccccctccc agacaggccc tccctgtctc cagggccccc accgaggttc 14700
ccagggctgg agacttcctc tggtaaacad tctccagcc tcccctcccc tggggacgcc 14760
aaggaggtgg gccacaccca ggaaggga aa gcgggcagcc ccgttttggg gacgtgaacg 14820
ttttaataat ttttgctgaa ttctttacaa ctaaataaca cagatattct tataaataaa 14880
attgtaaaaa aaaaaa 14896

- 67 -

<210> 39

<211> 604

<212> DNA

<213> Homo sapiens

<400> 39

ccacgcgtcc gcgctgcgcc acatcccacc ggcoettaca ctgtgggtgtc cagcagcatc	60
cggcttcatg gggggacttg aaccctgcag caggctcctg ctctgcctc tctgctggc	120
tgtaagtggc ctccgtcctg tccaggccca ggcccagagc gattgcagtt gctctacggt	180
gagcccgggc gtgctggcag ggatcgtgat gggagacctg gtgctgacag tgctcattgc	240
cctggccgtg tacttcctgg gccggctggc ccctcggggg cgaggggctg cggaggcagc	300
gaccgcgaaa cagcgtatca ctgagaccga gtcgccttat caggagctcc agggtcagag	360
gtcggatgtc tacagcgacc tcaacacaca gaggccgtat tacaatgag cccgaatcat	420
gacagtcagc aacatgatac ctggatccag ccattcctga agcccaccct gcacctcatt	480
ccaactccta ccgcgataca gaccacaga gtgccatccc tgagagacca gaccgctccc	540
caatactctc ctaaaataaa catgaagcac aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	600
aaaa	604

<210> 40

<211> 1097

<212> DNA

<213> Homo sapiens

<400> 40

agagaagacg tgcagggacc ccgcgcacag gagctgccct cgcgacatgg gtcacccgcc	60
gctgctgccg ctgctgctgc tgctccacac ctgcgtccca gcctcttggg gcctgcgggtg	120
catgcagtgt aagaccaacg gggattgccg tgtggaagag tgcgccctgg gacaggacct	180
ctgcaggacc acgatcgtgc gcttgtggga agaaggagaa gagctggagc tgggtggagaa	240
aagctgtacc cactcagaga agaccaacag gacctgagc tatcggactg gcttgaagat	300
caccagcctt acogagggtg tgtgtggggt agacttgtgc aaccagggca actctggccg	360
ggctgtcacc tattcccga ggcgttacct cgaatgcatt tctgtggct catcagacat	420

- 68 -

gagctgtgag agggggccggc accagagcct gcagtgccgc agccctgaag aacagtgcct	480
ggatgtggtg acccactgga tccaggaagg tgaagaagg cgtccaaagg atgaccgcca	540
cctccgtggc tgtggctacc ttcccggctg cccgggctcc aatggtttcc acaacaacga	600
caccttcac ttctgaaat gctgcaacac caccaaagc aacgagggcc caatcctgga	660
gcttgaaaat ctgccgcaga atggccgcca gtgttacagc tgcaagggga acagcaccca	720
tggatgctcc tctgaagaga ctttcctcat tgactgccga ggcccatga atcaatgtct	780
ggtagccacc ggcactcacg aacgctcact ctggggaagc tggttgccat gtaaaagtac	840
tactgcctg agaccacat gctgtgagga agcccaagct actcatgtat aaatgccatg	900
tggagataga gcccagatg tttcagccat ctcagcccag gcaccagaca agtgggtgaa	960
gaagccacct tggacatgta gcccagcag atgtgatata gagaagaaac aggaaacttg	1020
gctatattag tttcctaggg ctgcctgtga taaattatta caaactttat aaaaaaaaaa	1080
aaaaaaaaaa aaaaaaa	1097

<210> 41

<211> 2631

<212> DNA

<213> Homo sapiens

<400> 41

ggcagcagga acaacctatt tgcaaagttg gcgcaaacat tcctgcctga caggaccatg	60
gacacagggt gtagagatag agatggctct ggctgtgcat tcagcagatt ctgtagatag	120
aattaatagg acttggatgg gattgtggtg agagaaagtg aaatgaaaga taagttctag	180
tttggaaagtt ttaacaactg aatgttttaa ctcaaataga cacaaaatat tggaagagtg	240
gcaggtttgg gaggatgaga caatcaactg tttggttgag ccacgtagg tttgaaatgt	300
ctacgggatc ccgtggggag aggttatatc agactggagc accagagaga ggccaaggct	360
gatagtttag atgaaaagag agcatgatat ttaagccct gagactggat aatatcacct	420
atagaaagac tatatagaga taagagaggt ggggaacaag taaaagctgc gggacactcc	480
taaatttaga gtcaaattta gagcagaaaa tactagcaaa ggggactgaa aagcgggtggc	540
caattgagct tcaaagtcaa gtgaaagtgt gttgtgtgta catttatcat ctcattggcac	600
aggaaaaacg tgatttaagg agaaggaagc gatccaatgg gaagaagaga tccaatggat	660
cctctatcac gaagatattg agataagaac caatatggat ttgcaccac tgcatttgca	720

- 69 -

gccttgaggt cataagcatc ctcaggaaaa tgcaccaggt gctgctggca agatggaaac	780
caacttctcc actcctctga atgaatatga agaagtgtcc tatgagtctg ctggctacac	840
tgttctgcgg atcctcccat tgggtggtgct tggggtcacc tttgtcctcg gggtcctggg	900
caatgggctt gtgatctggg tggctggatt ccggatgaca cgcacagtca ccaccatctg	960
ttacctgaac ctggccctgg ctgacttttc tttcacggcc acattaccat tcttcattgt	1020
ctccatggcc atgggagaaa aatggccttt tggctggttc ctgtgtaagt taattcacat	1080
cgtggtggac atcaacctct ttggaagtgt cttcttgatt ggtttcattg cactggaccg	1140
ctgcattttgt gtctgcac cagtctgggc ccagaaccac cgcactgtga gtctggccat	1200
gaaggtgatc gtcggacctt ggattcttgc tctagtctt accttgccag ttttctctt	1260
tttgactaca gtaactattc caaatgggga cacatactgt actttcaact ttgcatactg	1320
gggtggcacc cctgaggaga ggctgaaggt ggccattacc atgctgacag ccagagggat	1380
tatccggttt gtcattggct ttagcttgcc gatgtccatt gttgccatct gctatgggct	1440
cattgcagcc aagatccaca aaaagggcat gattaaatcc agcogtccct tacgggtcct	1500
cactgctgtg gtggcttctt tcttcactctg ttggtttccc tttcaactgg ttgcccttct	1560
gggcaccgtc tggctcaaag agatgttggt ctatggcaag tacaaaatca ttgacatcct	1620
ggttaaccca acgagctccc tggccttctt caacagctgc ctcaacccca tgctttacgt	1680
ctttgtgggc caagacttcc gagagagact gatccactcc ctgcccacca gtctggagag	1740
ggccctgtct gaggactcag ccccaactaa tgacacggct gccaatctctg cttcacctcc	1800
tgcagagact gagttacagg caatgtgagg atggggtcag ggatattttg agttctgttc	1860
atcctacct aatgccagtt ccagcttcat ctacccttga gtcatattga ggcattcaag	1920
gatgcacagc tcaagtattt attcaggaaa aatgcttttg tgtccctgat ttgggggctaa	1980
gaaatagaca gtcaggctac taaaatatta gtgttatttt ttgttttttg acttctgcct	2040
ataccctggg gtaagtggag ttgggaaata caagaagaga aagaccagtg gggatttgta	2100
agacttagat gagatagcgc ataataaggg gaagacttta aagtataaag taaaatgttt	2160
gctgtaggtt ttttatagct attaaaaaaa atcagattat ggaagttttc ttctattttt	2220
agtttgctaa gagttttctg tttctttttc ttacatcatg agtggacttt gcattttatc	2280
aaatgcattt tctacatgta ttaagatggc catattattc ttcttctttt atgtaaatca	2340
ttataaataa tgttcattaa gttctgaatg ttaaactact cttgaattcc tggaataaac	2400
cacacttagt cctgatgtac tttaaataatt tatatctcac aggagttggg tagaatttct	2460

- 70 -

gtgtttatgt ttatatactg ttatttcact ttttctacta tccttgctaa gttttcatag 2520
aaaataagga acaaagagaa acttgtaatg gtctctgaaa aggaattgag aagtaattcc 2580
tctgattctg ttttctggtg ttatatcttt attaaatatt cagaaaaatt c 2631

<210> 42

<211> 1109

<212> DNA

<213> Homo sapiens

<400> 42

gcggggcctg aggcggagac cggagagccc gcggcccggc cggaggcagc tcgggacagg 60
cttgagcggc ggggcgcgct gcccggcggc cggggatgcg ggaccggctg ccagacctga 120
cggcgtgtag gaagaatgat gatggagaca cagttgttgt gggtgagaaa gatcatttca 180
tggtatgattt cttccatcag gtggaggaga ttagaaacag tattgataaa ataactcaat 240
atgttgaaga agtaaagaaa aaccacagca tcattctttc tgcaccaaac ccggaaggaa 300
aaataaaaga agagcttgaa gatctgaaca aagaaatcaa gaaaactgcg aataaaattg 360
cagccaagtt aaaggctatt gaacaaagtt ttgatcagga tgagagtggg aaccggactt 420
cagtggatct tcggatacga agaaccagc attcggtgct gtctcggaag tttgtggaag 480
ccatggcggg gtacaatgag gcacagactc tgtttcggga gcggagcaaa ggccgcatcc 540
agcgccagct ggagataact gggagaacca ccacagacga cgagctagaa gagatgctgg 600
agagcgggaa gccatccatc ttcacttccg acattatata agattcacia attactagac 660
aagctctcaa tgaaatcgag tcacgtcaca aggacatcat gaagctggag accagcatcc 720
gagagttgca tgagatgttc atggacatgg ctatgtttgt ggagactcag ggtgaaatga 780
tcaacaacat agaaagaaat gttatgaatg ccacagacta tgtagaacac gctaaagaag 840
aaacaaaaaa agctatcaaa tatcagagca aggcaagaag gaaaaagtgg ataattattg 900
ctgtgtcagt ggttctgggt gtctatcgtc tatttggett gtcgttgga tatgttgtac 960
gcagtgctgc ctctctgcca ggggtggggaa attgatgttc attatatatga agtttgttta 1020
ttgattctca cacatcaaac caccaagatt cctgctgcaa tgaaccaaatt cagcatcctg 1080
tcatttcgtg aatgaatctc agacgctgt 1109

- 71 -

<210> 43

<211> 2943

<212> DNA

<213> Homo sapiens

<400> 43

gaagctggac tgcagctggt ttcaggaact tctcttgacg agaagagaga ccaaggaggc	60
caagcagggg ctgggccaga ggtgcccaaca tggggaaact gaggctcggc tcggaaaggt	120
gaagtaactt gtccaagatc acaaagctgg tgaacatcaa gttggtgcta tggcaaggct	180
gggaaactgc agcctgactt gggctgccct gatcatcctg ctgctccccg gaagtctgga	240
ggagtgcggg cacatcagtg tctcagcccc catcgtccac ctgggggata ccatcacagc	300
ctcctgcata atcaagcaga actgcagcca tctggacccg gagccacaga ttctgtggag	360
actgggagca gagcttcagc ccggggggcag gcagcagcgt ctgtctgatg ggacccagga	420
atctatcata accctgcccc acctcaacca cactcaggcc tttctctcct gctgcctgaa	480
ctggggcaac agcctgcaga tcttggaaca ggttgagctg cgcgcaggct accctccagc	540
cataccccac aacctctcct gcctcatgaa cctcacaacc agcagcctca tctgccagtg	600
ggagccagga cctgagaccc acctacccac cagcttcact ctgaagagtt tcaagagccg	660
gggcaactgt cagacccaag gggactccat cctggactgc gtgcccagg acgggcagag	720
ccactgctgc atcccacgca aacacctgct gttgtaccag aatatgggca tctgggtgca	780
ggcagagaat gcgctgggga ccagcatgtc cccacaactg tgtcttgatc ccatggatgt	840
tgtgaaactg gagcccccca tgctgcggac catggacccc agccctgaag cggccccctc	900
ccaggcaggc tgcctacagc tgtgctggga gccatggcag ccaggcctgc acataaatca	960
gaagtgtgag ctgcgccaca agccgcagcg tggagaagcc agctgggcac tgggtgggccc	1020
cctccccttg gaggcccttc agtatgaget ctgcgggctc ctcccagcca cggcctacac	1080
cctgcagata cgctgcatcc gctggcccct gcctggccac tggagcgact ggagccccag	1140
cctggagctg agaactaccg aacggggccc cactgtcaga ctggacacat ggtggcggca	1200
gaggcagctg gaccccagga cagtgcagct gttctggaag ccagtgcctc tggaggaaga	1260
cagcggacgg atccaaggtt atgtggtttc ttggagaccc tcaggccagg ctggggccat	1320
cctgcccctc tgcaaacacca cagagctcag ctgcaccttc cacctgcctt cagaagccca	1380
ggaggtggcc cttgtggcct ataactcagc cgggacctct cgccccaccc cgggtggtctt	1440

- 72 -

ctcagaaagc agaggcccag ctctgaccag actccatgcc atggcccagag accctcacag	1500
cctctgggta ggctgggagc ccccacatcc atggcctcag ggctatgtga ttgagtgggg	1560
cctgggcccc ccagcgcgca gcaatagcaa caagacctgg aggatggaac agaatgggag	1620
agccacgggg tttctgctga aggagaacat caggcccttt cagctctatg agatcatcgt	1680
gacteccttg taccaggaca ccatgggacc ctcccagcat gtctatgcct actctcaaga	1740
aatggctccc tcccatgccc cagagctgca tctaaagcac attggcaaga cctgggcaca	1800
gctggagtgg gtgcctgagc cccctgagct ggggaagagc ccccttacc actacacat	1860
cttctggacc aacgctcaga accagtcctt ctccgccatc ctgaatgcct cctcccgtgg	1920
ctttgtcctc catggcctgg agcccgccag tctgtatcac atccacctca tggctgccag	1980
ccaggctggg gccaccaaca gtacagtcct caccctgatg accttgaccc cagaggggtc	2040
ggagctacac atcatcctgg gcctgttcgg cctcctgctg ttgctcacct gcctctgtgg	2100
aactgcctgg ctctgttgca gcccacacag gaagaatccc ctctggccaa gtgtoccaga	2160
cccagctcac agcagcctgg gctcctgggt gccacacatc atggaggagg atgccttcca	2220
gctgcccggc cttggcacgc caccatcac caagctcaca gtgctggagg aggatgaaaa	2280
gaagccggtg ccctgggagt ccataacag ctacagagacc tgtggcctcc ccactctggt	2340
ccagacctat gtgtccagg gggacccaag agcagtttcc acccagcccc aatcccagtc	2400
tggcaccagc gatcaggtec tttatgggca gctgctgggc agccccacaa gccaggggc	2460
agggcactat ctccgctgtg actccactca gccctcttg gcgggcctca ccccagccc	2520
caagtcctat gagaacctct ggttccaggc cagccccttg gggacctgg taaccccagc	2580
ccaagccag gaggacgact gtgtcttttg gccactgctc aacttcccc tctgcaggg	2640
gatccgggtc catgggatgg aggcgctggg gagcttctag ggcttcttg ggttcccttc	2700
ttgggcctgc ctcttaaagg cctgagctag ctggagaaga ggggagggtc cataagccca	2760
tgactaaaaa ctaccccagc ccaggtcttc accatctcca gtcaccagca tctcctctc	2820
ctcccaatct ccataggctg ggctcccag gcgatctgca tactttaagg accagatcat	2880
gctccatcca gcccaccca atggcctttt gtgcttggtt cctataactt cagtattgta	2940
aac	2943

- 73 -

<210> 44

<211> 1700

<212> DNA

<213> Homo sapiens

<400> 44

gccgaggctg cctgactgga atgagggtag ctgcggcgac tgcggcggct ggagcggggc	60
cggccatggc ggtgtggacg cgggccacca aagcggggct ggtggagctg ctcttgaggg	120
agcgttgggt cegagtgggt gccgagctga gcggggagag cctgagcctg acgggcgacg	180
ccgcgcggc cgagctggag cccgctctgg gaccgcggc cgccgccttc aacggcctcc	240
caaacggcgg cggcgcgggc gactcgctgc ccgggagccc aagccgcggc ctggggcccc	300
cgagcccgcg ggcgcgcct cggggccccg cgggtgaggc gggcgcgtcg ccgcccgtgc	360
gccgggtgcg ggtggtgaag caagaggcgg gcggcctggg catcagcatc aagggcggcc	420
gcgagaaccg gatgccgatc ctcatctcca agatcttccc cgggctggct gccgaccaga	480
gccgggcgct gcggctgggc gacgccatcc tgtcggtgaa cggcaccgac ctgcgccagg	540
ccaccacga ccaggccgtg caggcgctga agcgcgggg caaggagggtg ctgctggagg	600
tcaagtcat ccgagaagta acaccatata tcaagaagcc atcattagta tcagatctgc	660
cgtgggaagg tgcagcccc cagtcaccaa gcttttagtgg cagtgaggac tctgggtcgc	720
caaaacacca gaacagcacc aaggacagga agatcatccc tctcaaaatg tgctttgctg	780
ctagaaacct aagcatgccg gatctggaaa acagattgat agagctacat tctcctgata	840
gcaggaacac gttgatccta cgctgcaaag atacagccac agcacactcc tggttcgtag	900
ctatccacac caacataatg gctctcctcc cacagggtgtt ggctgaactc aacgccatgc	960
ttggggcaac cagtacagca ggaggcagta aagaggtgaa gcatattgcc tggctggcag	1020
aacaggcaaa actagatggt ggaagacagc aatggagacc tgtcctcatg gctgtgactg	1080
agaaggattt gctgctctat gactgtatgc cgtggacaag agatgcctgg gcgtcaccat	1140
gccacagcta cccacttggt gccaccaggt tggttcatte tggtccgga tgctgatccc	1200
cctcccttgg atctgacctt acatttgcta ccaggacagg ctctcgacag ggcattgaga	1260
tgcatctctt cagggtggag acacatcggg atctgtcate ctggaccagg atacttggtc	1320
agggttgcca tgctgctgct gagctgatca aggaagtctc tctaggctgc atgttaaagt	1380
gccaagaggt gaggcttact attcactatg aaaatgggtt caccatctca agggaaaatg	1440

- 74 -

gaggctccag cagcatattg tacgctacc cctttgaaag gctgaagatg tctgctgatg 1500
 atggcatccg aaatctatac ttggattttg gtggtcccga gggagaactg accatggacc 1560
 tgcactcttg tccgaagccg attgtatttg tgttgcacac gtttttatcg gccaaagtca 1620
 ctcgatatggg actgcttgta tgagcaacaa aaaatcagaa aagagccttg actgtcacaa 1680
 gaaatatttc cacctccaaa 1700

<210> 45

<211> 943

<212> DNA

<213> Homo sapiens

<400> 45

gcccgcagca cctcctcgcc agcagccgtc cggagccagc caacgagcgg aaaatggcag 60
 acaatttttc gctccatgat gcgttatctg ggtctggaaa cccaaaccct caaggatggc 120
 ctggcgcatg ggggaaccag cctgctgggg cagggggcta cccaggggct tectatcctg 180
 gggcctaccc cgggcaggca ccccagggg cttatcctgg acaggcacct ccaggcgctt 240
 accctggagc acctggagct tatcccgag cacctgcacc tggagtctac ccagggccac 300
 ccagcggccc tggggcctac ccatcttctg gacagccaag tgccaccgga gectaccctg 360
 ccactggccc ctatggcgcc cctgctgggc cactgattgt gccttataac ctgcctttgc 420
 ctgggggagt ggtgcctcgc atgctgataa caattctggg cacggtgaag cccaatgcaa 480
 acagaattgc tttagatttc caaagaggga atgatgttgc cttccacttt aaccacgct 540
 tcaatgagaa caacaggaga gtcattgttt gcaatacaaa gctggataat aactggggaa 600
 gggaagaaag acagtcgggtt tcccatttg aaagtgggaa accattcaaa atacaagtac 660
 tggttgaacc tgaccacttc aaggttgcag tgaatgatgc tcaattgttg cagtacaatc 720
 atcgggttaa aaaactcaat gaaatcagca aactgggaat ttctggtgac atagacctca 780
 ccagtgttcc atataccatg atataatctg aaaggggcag attaaaaaaa aaaaaagaat 840
 ctaaacctta catgtgtaaa ggtttcatgt tcaactgtgag tgaaaatttt tacattcacc 900
 aatatccctc ttgtaagtca tctacttaat aaatattaca gtg 943

- 75 -

<210> 46

<211> 2001

<212> DNA

<213> Homo sapiens

<400> 46

```

ggccgcggtg gtggctgcgg cggcggcggc gggagcagca tggattgggg cactgagctg      60
tgggatcagt tcgaggtgct cgagcgccac acgcagtggg ggctggacct gttggacaga      120
tatgtaaagt tcgtgaaaga acgcaccgaa gtggaacagg cttacgccaa acaactgcgg      180
agcctggtga aaaaatatct gcccaagaga cctgccaaagg atgacacctga gtccaaattc      240
agccagcaac agtccttcgt acagattctc caggaggtga atgactttgc aggccagcgg      300
gagctggtgg ctgagaacct cagtgtccgt gtatgtcttg agctgaccaa gtactcacia      360
gagatgaaac aggagaggaa gatgcacttc caagaagggc ggcgggceca gcagcagctg      420
gaaaatggct ttaaacagct ggagaatagt aagcgtaaata ttgagcggga ctgccgggag      480
gcagagaagg cagcccagac tgctgaacgg ctagaccagg atatcaacgc caccaaggct      540
gatgtggaga aggccaagca gcaagcccac cttcggagtc acatggccga agaaagcaaa      600
aacgaatatg cggctcaact gcagcgcttc aaccgagacc aagcccactt ctatttttca      660
cagatgcccc agatattcga taagctccaa gacatggatg aacgcagggc caccgcctg      720
ggtgccgggt atgggctcct gtcggaggcc gagctggagg tggtgcccat aatagccaag      780
tgcttgaggg gcatgaagggt ggctgcaaat gctgtggatc ccaagaacga ctcccacgtc      840
cttatagagc tgcacaagtc aggtttttgcc cgcccgggcg acgtggaatt cgaggacttc      900
agccagccca tgaaccgtgc accctccgac agcagtctgg gcacccccctc ggatggacgg      960
cctgaactcc gagggccggg tcgcagccgc accaagcgct ggcctttttg caagaagaac     1020
aagacagtgg tgaccgagga ttttagccac ttgccccag agcagcagcg aaaacggctt     1080
caacagcagt tggaagaacg cagtcgtgaa cttcagaagg aggttgacca gaggggaagcc     1140
ctaaagaaaa tgaaggatgt ctatgagaag acacctcaga tggggggacce cgccagcttg     1200
gagccccaga tcgctgaaac cctgagcaac attgaacggc tgaaattgga agtgcagaag     1260
tatgaggcgt ggctggcaga agctgaaagt cgagtcctta gcaaccgggg agacagcctg     1320
agccggcacg cccggcctcc cgaccccccc gctagcgccc cgccagacag cagcagcaac     1380
agcgcatac aggacaccaa ggagagctct gaagagcctc cctcagaaga gagccaggac     1440

```

- 76 -

```

acccccatTT acacggagtt tgatgaggat ttcgaggagg aaccacatc ccccataggt 1500
cactgtgtgg ccatctacca ctttgaaggg tccagcgagg gcactatctc tatggccgag 1560
ggtgaagacc tcagtottat ggaagaagac aaaggggacg gctggacccg ggtcaggcgg 1620
aaagagggag gcgagggcta cgtgcccacc tcctacctcc gagtcacgct caattgaacc 1680
ctgccagaga cgggaagagg ggggctgtcg gctgctgctt ctggggccacg gggagcccca 1740
ggacctatgc actttatttc tgaccccgctg gcttcggctg agacctgtgt aacctgctgc 1800
ccctccacc cccaaccag tcctacctgt cacaccggac ggacccgctg tgccttctac 1860
catcgttcca ccattgatgt acatactcat gttttacatc tttcttttct gcgctcggct 1920
cgggccatTT tgttttatac aaaaatgggt tttttttttt tctttaatat atttcaagag 1980
attttttttt tttttttttt t 2001

```

<210> 47

<211> 2038

<212> DNA

<213> Homo sapiens

<400> 47

```

gcaggccccgt tggaagtgggt tgtgacaacc ccagcaatgt ggagaagcct ggggcttgcc 60
ctggetctct gtctcctccc atcgggagga acagagagcc aggaccaaag ctctttatgt 120
aagcaacccc cagcctggag cataagagat caagatccaa tgctaaactc caatggttca 180
gtgactgtgg ttgctcttct tcaagccagc tgatacctgt gcatcatcga ggcattctaa 240
ttagaagacc tgcgagtaaa actgaagaaa gaaggatatt ctaatatctc ttatatgtt 300
gttaatcatc aaggaatctc ttctcgatta aaatacacac atcttaagaa taaggtttca 360
gagcatattc ctgtttatca acaagaagaa aaccaaacag atgtctggac tcttttaa 420
ggaagcaaag atgacttcct catatatgat agatgtggcc gtcttgata tcatcttgg 480
ttgccttttt ccttctaac tttcccatat gtagaagaag ccattaagat tgcttactgt 540
gaaaagaaat gtggaaactg ctctctcacg actctcaaag atgaagactt ttgtaaacgt 600
gtatctttgg ctactgtgga taaaacagtt gaaactccat cgcctcatta ccatcatgag 660
catcatcaca atcatggaca tcagcacctt ggcagcagtg agctttcaga gaatcagcaa 720
ccaggagcac caaatgctcc tactcatcct gctcctccag gccttcatca ccaccataag 780
cacaagggtc agcataggca gggtcaccca gagaaccgag atatgccagc aagtgaagat 840

```


- 77 -

```

ttacaagatt tacaaaagaa gctctgtcga aagagatgta taaatcaatt actctgtaaa    900
ttgcccacag attcagagtt ggctcctagg agctgatgct gccattgtcg acatctgata    960
tttgaaaaaa caggggtctgc aatcacctga cagtgtaaag aaaacctccc atctttatgt   1020
agctgacagg gacttcgggc agaggagaac ataactgaat cttgtcagtg acgtttgcct   1080
ccagctgcct gacaaataag tcagcagctt ataccacag aagccagtgc cagttgacgc   1140
tgaaagaatc aggcaaaaaa gtgagaatga ccttcaaact aaatatttaa aataggacat   1200
actccccaat ttagtctaga cacaatttca tttccagcat ttttataaac taccaaatta   1260
gtgaacccaa aatagaaatt agatttgtgc aaacatggag aaatctactg aattggcttc   1320
cagattttta attttatgtc atagaaatat tgactcaaac catatttttt atgatggagc   1380
aactgaaagg tgattgcagc ttttggttaa tatgtctttt tttttctttt tccagtgttc   1440
tatttgcttt aatgagaata gaaacgtaaa ctatgaccta ggggttttct gttggataat   1500
tagcagttta gaatggagga agaacaacaa agacatgctt tccatttttt cctttactta   1560
tctctcaaaa caatattact ttgtcttttc aatcttctac ttttaactaa taaaataagt   1620
ggattttgta ttttaagatc cagaaatact taacacgtga atattttgct aaaaaagcat   1680
atataactat tttaaataat catttatctt ttgtatatct aagactcatc ctgattttta   1740
ctatcacaca tgaataaagg cctttgtatc tttctttctc taatgttgta tcatactctt   1800
ctaaaacttg agtggctgtc ttaaaagata taaggggaaa gataatattg tctgtctcta   1860
tattgcttag taagtatttc catagtcaat gatggtttaa taggtaaacc aaaccctata   1920
aacctgacct cctttatggt taatactatt aagcaagaat gcagtacaga attggataca   1980
gtacggattt gtccaaataa attcaataaa aaccttaaaa aaaaaaaaaa aaaaaaaa   2038

```

<210> 48

<211> 3474

<212> DNA

<213> Homo sapiens

<400> 48

```

gcgcgccggc ggctcgggca gaggggcggg agctgaggcg ggagcggaca ggctgggtggg    60
cgagcgcgag gcgcggaatg gtggactacc acgcggcgaa ccagtcgtac cagtacggcc   120
ccagcagcgc ggcaatggct tggcggcggg ggagcatggg cgactacatg gccagaggag   180

```

- 78 -

acgactggga	ccgggacctg	ctgctggacc	cggcctggga	gaagcagcag	cgcaagacct	240
tcacggcatg	gagcaactcc	cacctgcgga	aggcaggcac	acagatcgag	aacattgatg	300
aggacttccg	agacgggctc	aagctcatgc	tgctcctgga	ggtcatatca	ggggagcggt	360
tacctaagcc	ggagcggggg	aagatgagag	tgacacaaat	caacaatgtg	aacaaagcgc	420
tggactttat	tgccagcaaa	gggatcaagc	tggacttcca	tcgggcagaa	gagattgtgg	480
acggcaacgc	aaagatgacc	ctgggaatga	tctggaccat	catccttagg	ttcgccatcc	540
aggacatctc	cgtggaagag	acctcggcca	aggaagggct	ccttctctgg	tgccagagaa	600
agacagcccc	atataagaac	gtcaatgtgc	agaacttcca	catcagctgg	aaggatggtc	660
ttgccttcaa	tgccctgatc	caccggcaca	gaccagagct	gattgagtat	gacaagctga	720
ggaaggacga	ccctgtcacc	aacctgaaca	atgccttcga	agtggctgag	aaatacctcg	780
acatccccaa	gatgctggat	gcagaggaca	tcgtgaacac	ggcccggccc	gacgagaagg	840
ccataatgac	ctatgtgtcc	agcttctacc	atgccttttc	aggagcgcag	aaggctgaaa	900
ctgaaactgc	cgccaaccgg	atctgtaagg	tgctggctgt	caaccaagag	aactgcagca	960
cctcgatgga	ggactacgag	aagctggcca	gcgacctcct	ggagtggatc	cggcgcacca	1020
tcccctggct	ggaggaccgt	gtgccccaaa	agactatcca	ggagatgcag	cagaagctgg	1080
aggacttccg	cgactaccgg	cgtgtgcaca	agccgcccac	ggtgcaggag	aagtgccagc	1140
tggagatcaa	cttcaacagc	gtgcagacca	agctgcgcct	cagcaaccgg	cccgccttca	1200
tgccctccga	gggcaagatg	gtctcggaca	tcaacaatgg	ctggcagcac	ttggagcagg	1260
ctgagaaggg	ctacgaggag	tggtgctga	atgagattcg	caggctggag	cggctcgacc	1320
acctggcaga	gaagttccgg	cagaaagcct	ccatccacga	ggcctggact	gacgggaagg	1380
aagccatgct	gaagcaccgg	gactacgaga	cggccacact	atcggacatc	aaagccctca	1440
ttcgcaagca	cgaggccttc	gagagcgacc	tggtgcgca	ccaggaccgc	gtggagcaga	1500
tcgccgcctc	cgccaggag	ctcaacgagc	tggattacta	cgactcccac	aatgtcaaca	1560
cccggtgcca	gaagatctgt	gaccagtggg	acgccctcgg	ctctctgaca	catagtcgca	1620
gggaagccct	ggagaaaaca	gagaagcagc	tggaggccat	catcgaccag	ctgcacctgg	1680
aatacgccaa	gcccgcggcc	cccttcaaca	actggatgga	gagcgccatg	gaggacctcc	1740
aggacatgtt	catcgtccat	accatcgagg	agattgaggg	cctgatctca	gcccatgacc	1800
agttcaagtc	caccctgccg	gacgcccata	gggagcgcga	ggccatcctg	catccacaag	1860
gaggccagag	gatcgctgag	agcaaccaca	tcaagctgtc	gggcagcaac	ccctacacca	1920
ccgtcacccc	gcaaatacatc	aactccaagt	gggagaaggt	gcagcagctg	gtgccaaaac	1980

- 79 -

```

gggaccatgc cctcctggag gagcagagca agcagcagca gtccaacgag cacctgcgcc 2040
gccagttcgc cagccaggcc aatgttgtgg ggccctggat ccagaccaag atggaggaga 2100
tcgcgatctc cattgagatg aacgggaccc tggaggacca gctgagccac ctgaagcagt 2160
atgaacgcag catcgtggac tacaagccca acctggacct gctggagcag cagcaccagc 2220
tcatccagga ggccctcatc ttcgacaaca agcacaccaa ctataccatg gagcacatcc 2280
gcgtgggctg ggagcagctg ctcaccacca ttgcccgcac catcaacgag gtggagaacc 2340
agatccttac ccgcgacgcc aagggcatca gccaggagca gatgcaggag ttccgggcgt 2400
ccttcaacca cttcgacaag gatcatggcg gggcgctggg gcgaggagtt caaggcctgc 2460
ctcatcagcc tgggctacga cgtggagaac gaccggcagg tgaggccgag ttcaaccgca 2520
tcatgagcct ggtcgacccc aaccatagcg gccttggttac cttccaagcc ttcatcgact 2580
tcatgtcgcg ggagaccacc gacaccgaca cggctgacca ggtaatcact tccttcaagg 2640
tcctagcagg ggacaagaac ttcatcacag ctgaggagct gcggagagag ctgccccccg 2700
accaggccga gtactgcac gcccgcatgg cgccatacca gggccctgac ggcgtgcgcg 2760
gtgccctcga ctacaagtcc ttctccacgg ccttgatatg cgagagcgac ctgtgaggcc 2820
ccagagacct gacccaacac ccccgacgcc tccaggagcc tggcagcccc acagtcccat 2880
tcctccacte tgtatctatg caaagcacte tctctgcagt ctccgggggtg ggtgggtggg 2940
cagggagggg ctggggcagg ctctctctc tctctctttg tgggttggec aggaggttcc 3000
cccgaccagg ttggggagac ttggggccag cgcttctggt ctggtaaata tgtatgatgt 3060
gttgtgettt ttttaaccaag gaggggcccag tggattccca cagcacaacc ggtcccttcc 3120
atgccctggg atgcctcacc acaccaggt ctcttctctt gctctgaggt cccttcaagg 3180
cctccccaat ccaggccaaa gcccctatgt ccttggtccag ggaactgcct gggccatgcg 3240
aggggcccagc agagggcgcc accacctgac ggctgggacc cacccagccc ctctcccctc 3300
tctgctccag actcaactgc cattgccagg agatggcccc aacaagcacc ccgcttttgc 3360
agcagaggag ctgagttggc agaccgggccc cccctgaacc gcaccccatc ccaccagccc 3420
cggccttgct ttgtctggcc tcacgtgtct cagattttct aagaacccaa aaaa 3474

```

- 80 -

<210> 49

<211> 1466

<212> DNA

<213> Homo sapiens

<400> 49

```

ggttctgccc tgctgtcctc tgccacccta acagcccact tgacgaggag aatctgaccc      60
aggagaacca agaccgaggg acacacgtgg acctcggatt agcctccgcc aacgtggact      120
tcgctttcag cctgtacaag cagttagtcc tgaaggcccc tgataagaat gtcattctct      180
ccccactgag catctccacc gccttggcct tctgtctctt gggggcccat aataccaccc      240
tgacagagat tctcaaaggc ctcaagttca acctcacgga gacttctgag gcagaaattc      300
accagagctt ccagcacctc ctgcgcaccc tcaatcagtc cagcgatgag ctgcagctga      360
gtatgggaaa tgccatgttt gtcaaagagc aactcagttt gctggacagg ttcacggagg      420
atgccaagag gctgtatggc tccgaggcct ttgccactga ctttcaggac tcagctgcag      480
ctaagaagct catcaacgac tacgtgaaga atggaactag ggggaaaatc acagatctga      540
tcaaggacct tgactcgcag acaatgatgg tcttgggtgaa ttacatcttc tttaaagcca      600
aatgggagat gccctttgac cccaagata ctcacagtc aaggttctac ttgagcaaga      660
aaaagtgggt aatggtgccc atgatgagtt tgcacacact gactatacct tacttccggg      720
acgaggagct gtctgcacc gtggtggagc tgaagtacac aggcaatgcc agcgcactct      780
tcacctccc tgatcaagac aagatggagg aagtggaagc catgctgctc ccagagaccc      840
tgaagcgggt gagagactct ctggagttca gagagatagg tgagctctac ctgccaaagt      900
tttccatctc gagggactat aacctgaacg acatacttct ccagctgggc attgaggaag      960
ccttcaccag caaggctgac ctgtcaggga tcacaggggc caggaacctc gcagtctccc     1020
aggtggtcca taaggctgtg cttgatgtat ttgaggaggg cacagaagca tctgctgcca     1080
cagcagtcaa aatcacctc ctttctgcat tagtggagac aaggaccatt gtgcgtttca     1140
acaggccctt cctgatgatc attgtcccta cagacacca gaacatcttc ttcagtagca     1200
aagtcaccaa tccaagcaa gcctagagct tgccatcaag cagtggggct ctcagtaagg     1260
aacttggaat gcaagctgga tgctgggtc tctgggcaca gcctggcccc tgtgcaccga     1320
gtggccatgg catgtgtggc cctgtctgct tctcctcgga aggtgacagc gattccctgt     1380
gtagctctca catgcacagg ggcccatgga ctcttcagtc tggagggtcc tgggcctcct     1440

```

- 81 -

gacagcaata aataatttcg ttggcc 1466

<210> 50

<211> 1519

<212> DNA

<213> Homo sapiens

<400> 50

cagccccctgc	tttccctagt	tccagttcca	agatggggaa	atccttcgcc	aacttcatgt	60
gcaagaaaga	ctttcatcct	gcctccaaat	ccaatatcaa	aaaagtatgg	atggcagaac	120
agaaaatatc	atatgataag	aagaaacaag	aagaattgat	gcagcaatat	cttaaagaac	180
aagaatcata	tgataataga	ttgcttatgg	gagatgaacg	tgtaaagaat	ggccttaatt	240
tcatgtatga	agccccacca	ggagctaaaa	aagaaaacaa	agagaaagaa	gaaacagaag	300
gagagaccga	atacaaattt	gaatggcaga	aaggagcccc	acgagaaaaa	tatgccaaag	360
atgacatgaa	catcagagat	cagccctttg	gtattcaggt	tcgaaatgtg	aggtgcatta	420
aatgtcacia	atgggtcatg	tcaacacaga	tcgagaatgt	cctttgtttg	gtctttcttg	480
aagtcaatgc	aagttcgggt	cccactgatg	gctcagggcc	atcgatgcac	ccctcggagc	540
taataggcga	gatgagaaac	cagtgggttt	gcactgaaac	gaaatgtact	ggggagaaac	600
ttgaccgcaa	actgatccat	cacaggagta	tgttgcaagt	gcagggtgaa	gaagatccag	660
aagttgaatt	tttaaagtca	ctaacaacca	aacaaaaaca	gaaacttctc	aggaaattag	720
atcgactgga	gaagaaaaaa	aagaaaaaag	atagaaaaaa	gaaaaagttt	cagaagagca	780
gaagtaaaca	caaaaaacat	aagtcctctt	cttcctatct	tcctcctcct	cctcctcttc	840
ctctactgag	acttcagaaa	gcagtagtga	gagtgagagt	aacaataaag	aaaaaaaaac	900
tacaaaggaa	gaaaagaaag	aaaaacaagt	gttcagggca	taacaacagt	gattctgaag	960
agaaggacaa	gtctaagaag	agaaagcttc	atgaagaact	ttctagcact	caccataacc	1020
gggaaaaaagc	caaggaaaag	cccaggttct	taaaacacga	gagttctagg	gaggacagca	1080
aatggagcca	ttctgattct	gacaaaaagt	ccagaacca	taaacatagc	ccagagaaga	1140
gaggctctga	aagaaaggag	gggagcagca	gaagccacgg	caggaggagaa	aggagccgga	1200
gaagccagcc	agaagtcctg	gtagttacaa	gcaaagggag	acaaggaaac	gggcacagcg	1260
aacatcctgg	tgaagagcaa	agcagaagaa	atgacagcag	aagccatggc	acagacttgt	1320
atagaggaga	aaaaatgtac	agagagcacc	caggaggtac	acatactaaa	gtgacacaaa	1380

- 82 -

gagaatgaag cagaagtaga gaagaaagac tgtatgtgac aattacctgg gaataaaaaat 1440
 atctccactt ttttattgaa taccttttagc aaggggtaaa ttatatactg ttgtctttct 1500
 aataaaaaag ctcaattttt 1519

<210> 51

<211> 2074

<212> DNA

<213> Homo sapiens

<400> 51

cacaaggcgg tagccatggc ggaggcggcg gctgcagcgg gtgggactgg cttgggcgcg 60
 ggcgcgagct acgggtctgc agcggaccgg gaccgggacc cggacccgga ccgcgcgggg 120
 cggaggctgc gggttctctc tggccatctg ctgggcggcg cccgggagge tctgagtacc 180
 aatgagtgca aagcgcggag agcgcgctcg gcggccacgg cagcgcgccac ggccactccc 240
 gccgcgcagg agtcgggcac catcccaaag aagcggcaag aagttatgaa atggaatgga 300
 tggggatata atgattctaa attcatcttc aataagaagg gccaaattga attgactggg 360
 aaaagggtacc ctcttagtgg catgggttta ccaacattta aagaatggat ccaaaatacc 420
 cttggagtaa atgtggagca taaaactacc tctaaagcat ccttaaattcc tagtgataca 480
 cctccttctg ttgtaaataga agattttctt catgacctta aagaaactaa tatttcatat 540
 tcacaagagg cagatgatcg agtatctaga gctcatggtc attgtcttca tgagatatatt 600
 ttgctcaggg aaggaatggt tgagcgaatt cctgatatag ttttatggcc aacatgccat 660
 gatgatgtag ttaagattgt gaatctagct tgcaaatata atctttgtat cataccaatt 720
 ggtggaggaa caagtgtttc atatggcctg atgtgtcctg cagatgagac aagaacaatt 780
 atttcttttg acacttcaca aatgaatcga attctctggg ttgatgagaa caatttgaca 840
 gctcatgtgg aggctggcat aacaggacaa gagttggaaa gacagcttaa agaaagtggg 900
 tattgtacag gtcatgaacc agattccctg gagttcagta ctgtaggagg atgggtatct 960
 actcgcgcac caggcatgaa gaagaatatc tatggcaata tcgaggacct ggtgggttcac 1020
 ataaaaatgg taacacctag aggtataata gaaaaaagct gtcaaggacc tcgtatgtca 1080
 acaggccctg atatccatca cttcatcatg ggatctgaag gaactcttgg tgtaataaca 1140
 gaagctacaa taaaaatcag accagtccct gaataccaaa agtatggctc agtagctttc 1200

- 83 -

cctaattttg aacaaggagt agcctgttta agagaaattg caaaacagag atgtgctccg	1260
gcatctattc gcctcatgga caacaagcag tttcagtttg gtcatgctct taaacctcag	1320
gtttcctcta tctttacatc atttttggac ggattaaaaa agttttatat taaaaagttt	1380
aaaggatttg acccaaatac gctaagtgtg gccacattac tgtttgaggg ggatcgtgag	1440
aaggttcttc aacatgaaaa acaagtgtat gatattgctg caaaatttgg tgggttgga	1500
gctggagaag ataatggaca gagagggttat ttgctgacct atgttattgc atacattcga	1560
gacttggctt tggaatacta tgtattagga gaatcttttg agacttctgc tccttgggac	1620
agggtggtag atctctgtag aaatgtaaaa gaaagaataa caagggaatg caaagagaag	1680
ggtgttcagt ttgctccttt ttctacatgc agggtgacgc agacttacga tgcaggtgct	1740
tgtatctact tctattttgc ctttaactac aggggaatta gtgaccact gaccgtattt	1800
gaacaaactg aggcagctgc tagagaagaa atccttgcta atggaggag cctgtcacat	1860
caccatggag tgggcaagtt acggaagcaa tggctaaagg aaagtatctc tgatgtcggc	1920
tttgggatgc tgaagtctgt caaggaatat gtggacccca ataacatctt tggaaacaga	1980
aaccttttat aaatccatta gtaccattac aaaaaaatgt caattttttt tttaagtttt	2040
caactgtggt tatactagta atcaaata tcat	2074

<210> 52

<211> 2861

<212> DNA

<213> Homo sapiens

<400> 52

ctgctcctgc gcggcagctg ctttagaagg tctcgagcct cctgtacctt cccagggatg	60
aaccgggcct tccctctgga aggcgagggg tcgggccaca gtgagcgagg gccagggcgg	120
tgggcgcgcg cagagggaaa ccggatcagt tgagagagaa tcaagagtag cggatgaggc	180
gcttgtgggg cgcggcccg ggcctcctcg gcgcgggctg ggagaaggag tgggcggagg	240
cgcgcagga ggctcccg ggcctggcgg gccggctggg ccccgggcgc agtggagaa	300
agggaacgggc ggtgcccggg tgggcgtcct ggccagctca ccttgccctg gcggctcgcc	360
ccgccggca cttgggagga gcagggcagg gcccgcgcc tttgcattct gggaccgccc	420
ccttcattc ccgggccagc ggcgagcggc agcgacggct ggagccgcag ctacagcatg	480
agagccggtg ccgctcctcc acgectgcgg acgcgtggcg agcggaggca gcgctgcctg	540

- 84 -

ttcgcgccat	gggggcaccg	tggggctcgc	cgacggcggc	ggcgggcggg	cggcgcgggt	600
ggcgccgagg	ccgggggctg	ccatggaccg	tctgtgtgct	ggcgcccgcc	ggcttgacgt	660
gtacggcgct	gatcacctac	gcttgctggg	ggcagctgcc	gccgctgcc	tgggcgtcgc	720
caaccccgtc	gcgaccggtg	ggcgtgctgc	tgtggtggga	gcccttcggg	gggcgcgata	780
gcgccccgag	gccgccccct	gaactgccggc	tgcgcttcaa	catcagcggc	tgccgcctgc	840
tcacgcaccg	cgcgctcctac	ggagaggctc	aggccgtgct	tttccaccac	cgcgacctcg	900
tgaagggggc	ccccgactgg	cccccgccct	ggggcatcca	ggcgcacact	gccgaggagg	960
tggatctgcg	cgtgttggac	tacgaggagg	cagcggcggc	ggcagaagcc	ctggcgacct	1020
ccagccccag	gcccccgggc	cagcgtggg	tttgatgaa	cttcgagtcg	ccctcgcact	1080
ccccggggct	gcgaagcctg	gcaagtaacc	tcttcaactg	gacgctctcc	taccgggcgg	1140
actcggacgt	ctttgtgcct	tatggctacc	tctaccccag	aagccacccc	ggcgacccgc	1200
cctcaggcct	ggccccgcca	ctgtccagga	aacaggggct	ggtggcatgg	gtggtgagcc	1260
actgggacga	gcgccaggcc	cgggtccgct	actaccacca	actgagccaa	catgtgaccg	1320
tggacgtgtt	cggcgggggc	gggcgggggc	agccggtgcc	cgaaattggg	ctcctgcaca	1380
cagtggcccc	ctacaagttc	tacctggctt	tcgagaactc	gcagcacctg	gattatatca	1440
ccgagaagct	ctgggcgaac	gcgttgctcg	ctggggcggt	gccggtggtg	ctgggcccag	1500
accgtgccaa	ctacgagcgc	tttgtgcccc	gcggcgccct	catccacgtg	gacgacttcc	1560
caagtgcctc	ctccctggcc	tcgtacctgc	ttttcctcga	ccgcaacccc	gcggtctatc	1620
gccgctactt	ccactggcgc	cggagctacg	ctgtccacat	cacctccttc	tgggacgagc	1680
cttggtgccg	ggtgtgccag	gctgtacaga	gggctgggga	ccggcccaag	agcatacggg	1740
acttggccag	ctggttcgag	cgggtgaagcc	gcgctccccct	ggaagcgacc	caggggaggc	1800
caagttgtca	gctttttgat	cctctactgt	gcatctcctt	gactgccgca	tcattgggagt	1860
aagttcttca	aacacccatt	tttgctctat	gggaaaaaaa	cgatttacca	attaatatta	1920
ctcagcacag	agatgggggc	ccggtttcca	tattttttgc	acagctagca	attgggctcc	1980
ctttgctgct	gatgggcata	attgtttagg	ggtgaaggag	ggggttcttc	ctcaccttgt	2040
aaccagtgc	gaaatgaaat	agcttagcgg	caagaagccg	ttgaggcggt	ttcctgaatt	2100
tccccatctg	ccacaggcca	tatttggggc	ccgtgcagct	tccaaatctc	atacacaact	2160
gttccccgatt	cacgtttttc	tggaccaagg	tgaagcaaat	ttgtggttgt	agaaggagcc	2220
ttgttggtgg	agagtgggaag	gactgtggct	gcagggtggga	ctttgttgtt	tggattcctc	2280

- 85 -

acagccttgg ctctgagaa aggtgaggag ggcagtccaa gaggggccgc tgacttcttt 2340
 cacaagtact atctgttccc ctgtcctgtg aatggaagca aagtgtctga ttgtccttgg 2400
 aggaaactta agatgaatac atgcgtgtac ctcactttac ataagaaatg tattcctgaa 2460
 aagctgcatt taaatcaagt cccaaattca ttgacttagg ggagttcagt atttaatgaa 2520
 accctatgga gaatttatcc ctttacaatg tgaatagtca tctcctaatt tgtttcttct 2580
 gtctttatgt ttttctataa cctggatttt tttaatcata ttaaaattac agatgtgaaa 2640
 ataaagcaga agcaaccttt ttccctcttc ccagaaaacc agtctgtgtt tacagacaga 2700
 agagaaggaa gccatagtgt cacttccaca caattattta tttcatgtct ttactggacc 2760
 tgaaatttaa actgcaatgc cagtcctgca ggagtgtgtg cattaccctc tgcagaacag 2820
 tgaaagggtat tgcactacat tatggaatca tgcaaaaaaa a 2861

<210> 53

<211> 2448

<212> DNA

<213> Homo sapiens

<400> 53

gggttggttc caagtctttg ctattgtgaa tagtgccgca ataaacatac gtgtgcatgt 60
 gtctttatag cagcatgatt tatagtcctt tgggtatata ccagtaatg ggatggctgg 120
 gttctagatc cctgaggaat cgccacattg acttgcacaa tgggttgaact agtttacagt 180
 cccaccaaca gtgtaaaagt gttectatct ctccacatcc tctcgggcac ctgttggttc 240
 ctgacttttt aatgattgcc attctaactg gtgtgagatg atatctcatt gtggttttga 300
 tttgcatttc tctgatggcc agtgatgggt agcatttttt catgtgtttt ttggetgcat 360
 aaatgtcttc ttttgagaag tgtctgttca tgattttttt ttttagacaa agtattagat 420
 cagatatatt tggggaaaaa tgctttgtga ttgcttggtt tgaatgggtga gcattgtatt 480
 ttgttttaag ttgttttctg gttgttatta cagctatgaa gtcttacact ccatatttca 540
 ttctcctgtg gagtgctgtt gggatagcga aggctgccaa aatcatcate gtgccgcaa 600
 ttatgtttga aagccatatg tacattttca agacgctagc ctcagccttg cacgagagag 660
 gccaccatac agtgttcctc ctctctgaag gcagagacat cgccccatct aatcattaca 720
 gcctccagcg ctaccagggt atctttaaca gtaccacctc agatgctttc ctacagtcca 780
 agatgoggaa tattttctct gggagattga cagcaatoga actgtttgac atactggatc 840

- 86 -

actatactaa gaactgtgac ctgatggttg gcaaccatgc cctgatccag ggtctgaaga	900
aagaaaaatt tgacctgctg ctggtggacc ctaatgatat gtgtggattt gtgatagctc	960
atcttttagg ggttaaatat gctgtatttt caactggcct ttggtatcct gctgaagtgg	1020
gtgctcctgc tccattagca tacgtcccag agtttaactc actcctcaca gaccgcatga	1080
acttgctgca aaggatgaaa aataccggtg tttacctcat ttccagatta ggggtcagct	1140
ttctggttct tcccaaatat gaaaggataa tgcagaagta caacctgctg ccggagaagt	1200
ccatgtatga tttggttcat ggggtccagcc tgtggatgct gtgtactgac gtagcactgg	1260
aattcccaag acccactctg cctaatgttg tttatgtagg aggaatccta accaaaccag	1320
ccagcccact accagaagat ctccaaagat gggtaaattg tgctaataaa catggctttg	1380
tcttggtgtc ttttgagct ggtgtcaagt atctgtcaga agacattgct aacaaactgg	1440
caggagctct ggggagattg cctcaaaaag tgatttggag gttttctgga cccaaaccaa	1500
agaatctagg aaacaacact aaactcatag aatggttacc acaaaatgac ctgcttgggc	1560
attcaaagat taaagccttc ctgagccatg gtggtttgaa cagtattttt gaaactatgt	1620
atcatggtgt gcctgtagtg ggaattccac tctttggaga ccattatgat actatgacca	1680
gagtacaggc aaaaggcatg gggatattgc tagaatggaa gacagttact gaaaaagagc	1740
tctatgaagc actagtgaag gttatcaata atcccagcta ccgtcagagg gctcagaagc	1800
tttcggaaat tcacaaggat caacctggtc acctgtcaa tcgaactatc tattggatag	1860
attatattat tcgtcacaat ggagcccatc acctacgtgc cgctgtccat cagatctcct	1920
tttgtcagta ttttttactg gatattgcct ttgtgctttt gcttggtgct gccttggtat	1980
actttctctt gtcttgggtg acaaaattta tctacagaaa aatcaaaagt ctgtggtcta	2040
gaaataagca tagcacagtt aatggacatt accacaatgg aatcctcaat ggcaagtaca	2100
aaagaaatgg ccatattaaa catgaaaaga aagtgaatg agccaacagc ccaggtgata	2160
gaaataaatt ggttcactca ttgaattttt attgctatta tttagtctaa cagctactaa	2220
aagtaaaaca tcagtaaaca attctaacat gcccttatga gactactaat gaaattctgt	2280
ggaattaaga tggctgtaaa aagcacaaac ctaaaatgca gaaatgtatt ttattcaaat	2340
actgatgtag agagtttttg cactgaacct tttagaagcc ttaattattt aaatcaattc	2400
agtgactgtg tcagacctta gttttaaatc ttgatatgtg cgtgtccc	2448

- 87 -

<210> 54

<211> 3018

<212> DNA

<213> Homo sapiens

<400> 54

```

gaattccggg ccaggcatgg tagcgcatcg ctgtaatccc agctactcgg gaaactgagg      60
tgggagaatc gattgaacct ggaagtggag gttgcggtga gccaaagatca tcctgtcgca      120
ctccagcctg ggcaacaaga gcgaaactcc atctcaaaaa gaaaaaaaaa gatatatatg      180
tgtgacttac aggtacaggt aaagttgctt ctggttttct gggtgttgca tggtatattcc      240
tatgcagcca caggtcttta tttcttact taagtgcctc caacttccca taacacaaat      300
taaggcatga tgaacatcct ctctgtgctg aacatcctgt gtatgtcact tcagaagcct      360
gtgtgacggg ttcttttagtc ttataccta ggggtgggat ttctgggtca taggacagta      420
atttatatatt atttcactaa gtattctctt tctctggctt ttgttacata ttacctgttt      480
gtcctccaga aaacttgcac caatttacat tcctaccaat agggtaggag agtgcacaat      540
gggtggattc taactccaaa tctaacacct cttcttttct ttgtttctag cagccatggc      600
aatgacaggc tcaacacctt gctcatccat gagtaaccac acaaaggaaa gggtgacaat      660
gaccaaagtg aactggaga atttttatag caaccttacc gctcaacatg aagaacgaga      720
aatgagacaa aagaagttag aaaaggtgat ggaagaagaa ggcctaaaag atgaggagaa      780
acgactccgg agatcagcac atgctcggaa ggaaacagag tttcttcggt tgaagagAAC      840
aagacttgga ttggaagatt ttgagtcctt aaaagtaata ggcagaggag catttggtga      900
ggtacggctt gttcagaaga aagatacggg acatgtgtat gcaatgaaaa tactccgtaa      960
agcagatatg cttgaaaaag agcagggttg ccacattcgt gcggagcgtg acattctagt     1020
ggaggcagac agtttgtggg ttgtgaaaat gttctatagt tttcaggata agctaaacct     1080
ctacctaate atggagtacc tgccctggagg ggacatgatg accttggtga tgaaaaaaga     1140
cactctgaca gaagaggaga ctcagtttta tatagcagaa acagtattag ccatagactc     1200
tattcaccaa cttggattca tccacagaga catcaaacca gacaaccttc ttttggacag     1260
caagggccat gtgaaacttt ctgactttgg tctttgcaca ggactgaaaa aagcacatag     1320
gacagaatatt tataggaatc tgaaccacag cctccccagt gatttcactt tccagaacat     1380
gaattccaaa aggaaagcag aaacctggaa aagaaataga cgtcagctag ccttctccac     1440

```

- 88 -

agtaggcact cctgactaca ttgctcctga ggtgttcatg cagaccgggt acaacaagct	1500
ctgtgattgg tggtcgcttg gggatgatcat gtatgagatg ctcatcggct acccaccttt	1560
ctgttctgag acccctcaag agacatataa gaaggatgat aactggaaag aaactttgac	1620
ttttcctcca gaagttccca tctctgagaa agccaaggat ctaattttga ggttctgctg	1680
tgaatgggaa catagaattg gagctcctgg agttgaggaa ataaaaagta actctttttt	1740
tgaaggcgtt gactgggaac atatcagaga gagacctgct gcaatatcta ttgaaatcaa	1800
aagcattgat gatacctcaa acttcgatga gtttccagaa tctgatattc ttaagccaac	1860
agtggccaca agtaatcatc ctgagactga ctacaagaac aaagactggg tcttcatcaa	1920
ttacacgtac aagcgctttg agggcctgac tgcaaggggg gcaatacctt cctacatgaa	1980
agcagcaaaa tagtactctt gccacggaat cctatgtgga gcagagtctt ttgtataaca	2040
tcatgctttt cctctcacac tcttgaagag cttccaagaa gttgatggaa cccaccaata	2100
tgtcatagta aagtctcctg aaatgtggta gtaagaggat tttcttccat aatgcactctg	2160
aaaaactgta aacaaagaca accattttcta ctacgtcggc cataaacagc tatectgctt	2220
tggaagagaa gcatcatgag ccaatttgat aggtgtttta aaaataactt gagttttcct	2280
aagttcatca gaatgaaggg gaaaaacagc catcatccaa cattattgag attgtcgtgt	2340
atagtcatcg aatatcagcc agttcctgta attttgtgac acgtctctctg ccaagccac	2400
caagtatttc ctttatagct aaaagttcca tagtactaag gaaataaagc aataaagaca	2460
gtctcagcag ccaggattct ggctgaagga aatgatccgc caccctgagg gtggatgatgg	2520
tagtttctac ccatacctca gcctcaggcg agtggcttat agcctccatt catggtgcac	2580
tttatattatg gtactaagat aaagactgtc aatccattga tttatctcct cctgtcccc	2640
atctaaaata cccatgctgc ttttctgagt gttgatgggg gttaccagct tgatccactg	2700
ttgctcttag aaggcccaga aagtctttgg gcattgcaag aaatcccga ttatgtggaa	2760
aaccctcact ttctcttcac ggctgtacca gaaaatccct aagacagatc ttgccgtgga	2820
ctagcaatac ctgcaagtgc tgccaatggg aactcaattt attcctggga acctaacgag	2880
gagagcccag gcctaggcag gaggcctgga accctcttgg ctaagggtgct gttcctgttc	2940
ctgcaaggtc tccagaaccc ctttggaat ggtgaaggaa ccagcccaat agaagtacag	3000
agccagctga cggaattc	3018

- 89 -

<210> 55

<211> 1750

<212> DNA

<213> Homo sapiens

<400> 55

gtggcgccg	tcgcccggat	cccctgagct	gcccgccatc	ccacgtgacc	gcgcccgc	60
ccagctccac	cgctgagccc	gtcgcgatg	gccctcttcg	gggcctctt	cctagcgctg	120
ctggcaggcg	cacatgcaga	gttcccaggc	tgcaagatcc	gcgtcacctc	caaggcgctg	180
gagctggtga	agcaggaggg	gtgcgcttt	ctggagcaag	agctggagac	tatcaccatt	240
ccggacctgc	ggggcaaaga	aggccacttc	tactacaaca	tctctgaggt	gaaggtcaca	300
gagctgcaac	tgacatcttc	cgagctcgat	ttccagccac	agcaggagct	gatgcttcaa	360
atcaccaatg	cctcettggg	gtgcgcttc	cggagacagc	tgtctactg	gttcttctat	420
gatgggggct	acatcaacgc	ctcagctgag	ggtgtgtcca	tccgcactgg	tctggagctc	480
tcccgggatc	ccgctggacg	gatgaaagtg	tccaatgtct	cctgccaggc	ctctgtctcc	540
agaatgcacg	cggccttcgg	gggaaccttc	aagaagggtg	atgattttct	ctccacgttc	600
atcacctcag	ggatgcgctt	cctcctcaac	cagcagatct	gccctgtcct	ctaccacgca	660
gggacgggtcc	tgtcaactc	cctcctggac	accgtgcctg	tgcgcagttc	tgtggacgag	720
cttgttgga	ttgactattc	cctcatgaag	gacctgtgg	cttccaccag	caacctggac	780
atggacttcc	ggggggcctt	cttccccctg	actgagagga	actggagcct	ccccaacggg	840
gcagtggagc	cccagctgca	ggaggaagag	cggatggtgt	atgtggcctt	ctctgagttc	900
ttcttcgact	ctgccatgga	gagctacttc	cgggcggggg	ccctgcagct	gttgctggtg	960
ggggacaagg	tgccccacga	cctggacatg	ctgctgaggg	ccacctactt	tgggagcatt	1020
gtcctgctga	gcccagcagt	gattgactcc	ccattgaagc	tggagctgcg	ggtcctggcc	1080
ccaccgcgct	gcaccatcaa	gccctctggc	accaccatct	ctgtcactgc	tagcgtcacc	1140
attgccctgg	tcccaccaga	ccagcctgag	gtccagctgt	ccagcatgac	tatggacgcc	1200
cgtctcagcg	ccaagatggc	tctccggggg	aaggccctgc	gcacgcagct	ggacctgcgc	1260
aggttccgaa	tctattccaa	ccattctgca	ctggagtcgc	tggctctgat	cccattacag	1320
gcccctctga	agaccatgct	gcagattggg	gtgatgccca	tgctcaatga	gcggacctgg	1380
cgtgggggtgc	agatcccact	acctgagggc	atcaactttg	tgcattgaggt	ggtgacgaac	1440

- 90 -

catgcgggat tcctcaccat cggggctgat ctccactttg ccaaagggct gcgagaggtg 1500
 attgagaaga accggcctgc tgatgtcagg gcgtccactg ccccccacacc gtccacagca 1560
 gctgtctgag ccctcaatcc ccaagctggc agctgtcatt caggacccca acccctctca 1620
 gcccctcttt tcccacattc atagcctgta gtgccccctc taacccccag tgccacagag 1680
 aagacgggat ttgaagctgt acccaattta attccataat caatctatca attacagtcc 1740
 gtccaccacc 1750

<210> 56

<211> 3288

<212> DNA

<213> Homo sapiens

<400> 56

cttcctctcc acgcggttga gaagacoggt cggcctgggc aacctgcgct gaagatgccg 60
 ggaaaactcc gtagtgacgc tggtttgga tcagacaccg caatgaaaaa aggggagaca 120
 ctgcgaaagc aaatcgagga gaaagagaaa aaagagaagc caaatctga taagactgaa 180
 gagatagcag aagaggaaga aactgttttc cccaaagcta aacaagttaa aaagaaagca 240
 gagccttctg aagttgacat gaattctcct aaatccaaaa aggcaaaaaa gaaagaggag 300
 ccatctcaaa atgacatttc tctaaaacc aaaagtttga gaaagaaaaa ggagcccatt 360
 gaaaagaaag tggtttcttc taaaaccaa aaagtgacaa aaaatgagga gccttctgag 420
 gaagaaatag atgctcctaa gcccaagaag atgaagaaag aaaaggaaat gaatggagaa 480
 actagagaga aaagccccaa actgaagaat ggatttctc atcctgaacc ggactgtaac 540
 ccagtgagag ctgccagtga agaaagtaac agtgagatag agcaggaaat acctgtggaa 600
 caaaaagaag gcgctttctc taattttccc atatctgaag aaactattaa acttctcaaa 660
 ggccgaggag tgaccttcct atttcctata caagcaaaga cattccatca tgtttacagc 720
 gggaaggact taattgcaca ggcacggaca ggaactggga agacattctc ctttgccatc 780
 cctttgattg agaaacttca tggggaactg caagacagga agagaggccg tgcccctcag 840
 gtactggttc ttgcacctac aagagagttg gcaaatcaag taagcaaaga cttcagtgac 900
 atcacaaaaa agctgtcagt ggcttgtttt tatggtggaa ctccctatgg aggtcaattt 960
 gaacgcatga ggaatgggat tgatatcctg gttggaacac caggtcgtat caaagaccac 1020
 atacagaatg gcaaactaga tctcaccaaa cttaagcatg ttgtcctgga tgaagtggac 1080

cagatggttg	atatgggatt	tgctgatcaa	gtggaagaga	ttttaagtgt	ggcatacaag	1140
aaagattctg	aagacaatcc	ccaaacattg	cttttttctg	caacttgccc	tcattgggta	1200
tttaatggtg	ccaagaaata	catgaaatct	acatatgaac	aggtggacct	gattggtaaa	1260
aagactcaga	aaacggcaat	aactgtggag	catctggcta	ttaagtgcc	ctggactcag	1320
agggcagcag	ttattgggga	tgtcatccga	gtatatagt	gtcatcaagg	acgcactatc	1380
atcttttgtg	aaaccaagaa	agaagcccag	gagctgtccc	agaattcagc	tataaagcag	1440
gatgctcagt	ccttgcatgg	agacattcca	cagaagcaaa	gggaaatcac	cctgaaaggt	1500
tttagaaatg	gtagttttgg	agttttgggtg	gcaaccaatg	ttgctgcacg	tgggttagac	1560
atccctgagg	ttgatttggt	tatacaaagc	tctccaccaa	aggatgtaga	gtcctacatt	1620
catcgatccg	ggcggacagg	cagagctgga	aggacggggg	tgtgcatctg	cttttatcag	1680
cacaaggaag	aatatcagtt	agtacaagt	gagcaaaaag	cgggaattaa	gttcaaacga	1740
ataggtgttc	cttctgcaac	agaaataata	aaagcttcca	gcaaagatgc	catcaggctt	1800
ttggattccg	tgcctcccac	tgccattagt	cacttcaaac	aatcagctga	gaagctgata	1860
gaggagaagg	gagctgtgga	agctctggca	gcagcactgg	cccatatttc	aggtgccacg	1920
tccgtagacc	agcgtcctt	gatcaactca	aatgtggggt	ttgtgaccat	gatcttgcag	1980
tgctcaattg	aatgccaaa	tattagttat	gcttggaag	aacttaaaga	gcagctgggc	2040
gaggagattg	attccaaagt	gaagggaatg	gtttttctca	aaggaaagct	gggtgtttgc	2100
tttgatgtac	ctaccgcac	agtaacagaa	atacaggaga	aatggcatga	ttcacgacgc	2160
tggcagctct	ctgtggccac	agagcaacca	gaactggaag	gaccacggga	aggatatgga	2220
ggcttcaggg	gacagcggga	aggcagtcga	ggcttcaggg	gacagcggga	cggaaacaga	2280
agattcagag	gacagcggga	aggcagtaga	ggcccagag	gacagcgatc	aggagggtggc	2340
aacaaaagta	acagatccca	aaacaaaggc	cagaagcgga	gtttcagtaa	agcatttggt	2400
caataattag	aatagaaga	tttatatagc	aaaaagagaa	tgatgtttgg	caatatagaa	2460
ctgaacatta	tttttcatgc	aaagttaaaa	gcacattgtg	cctccttttg	accacttgcc	2520
aagtcctgt	ctctttcaga	cacagacaag	cttcatttaa	attatttcat	ctgatcatta	2580
tcattttataa	ctttattggt	acttcttcat	cagtttttcc	ttttgaaagg	tgtatgaatt	2640
cattacattt	ttattcta	gtattatctg	tagattagaa	gataaaatca	agcatgtatc	2700
tgcctatact	ttgtgagttc	acctgtcttt	atactcaaaa	gtgtccctta	atagtgtcct	2760
tccctgaaat	aaatacctaa	gggagtgtaa	cagtctctgg	aggaccactt	tgagcctttg	2820

- 92 -

gaagttaagg	tttctcagc	cacctgccga	acagtttctc	atgtggctct	attatttgtc	2880
tactgagact	taatactgag	caatgttttg	aaacaagatt	tcaaactaat	ctgggttgta	2940
atacagttta	taccagtgtg	tgctctagac	ttggaagatg	tagtatgttt	gatgtggatt	3000
acctatactt	atgttcgttt	tgatacattt	ttagcttctc	attataaggt	gattcatgct	3060
ttagtgaatt	cttatagatg	atatataaaa	gtacatttta	atagaagcca	gggtttaagg	3120
aatttcacat	gtataaggtg	gctccatagc	tttatttgta	agtaggctgg	ataaatgggtg	3180
cttaaatggt	aatgtactcc	acttcttccc	attggaagat	taacattatt	taccaagaag	3240
gacttaaggg	agtagggggc	gcagattagc	attgctcaag	agtatgga		3288

<210> 57

<211> 863

<212> DNA

<213> Homo sapiens

<400> 57

tagatatattt	tcaaaaatac	agtgatgtca	ttgcaggaca	attttatgga	cacactcaca	60
gagacagcat	tatggttctt	tcagataaaa	aaggaagtcc	agtaaattct	ttgtttgtgg	120
ctctgctgt	tacaccagtg	aagagtgttt	tagaaaaaca	gaccaacaat	cctgggtatca	180
gactgtttca	gtatgatcct	cgtgattata	aattattgga	tatgttgcag	tattacttga	240
atctgacaga	ggcgaatcta	aaggagagat	ccatctggaa	gctggagtat	atcctgaccc	300
agacctacga	cattgaagat	ttgcagccgg	aaagtttata	tggattagct	aaacaattta	360
caatcctaga	cagtaagcag	tttataaaaat	actacaatta	cttctttgtg	agttatgaca	420
gcagtgtaac	atgtgataag	acatgtaagg	cctttcagat	ttgtgcaatt	atgaatcttg	480
ataatatattc	ctatgcagat	tgccctcaaac	agctttatat	aaagcacaaa	tactagtatt	540
tcacagtttt	tgctaataga	aaatgctgat	tctgattctg	agatcaattt	gtgggaattt	600
tacataaatc	tttgtaatt	actgagtggg	caagtagact	tcctgtcttt	gctttctttt	660
tttttttctt	tttgatgcct	taatgtagat	atctttatca	ttctgaattg	tattatatat	720
ttaaagtgct	cattaataga	atgatggatg	taaattggat	gtaaatatte	agtttatata	780
attatatcta	atttgtaccc	ttgttgaaat	tgtcatttat	acaataaage	gaattcttta	840
tctctaaaaa	aaaaaaaaaa	aaa				863

- 93 -

<210> 58

<211> 5177

<212> DNA

<213> Homo sapiens

<400> 58

ggactgcgaa	aggagcaggg	ttgcggagct	agggctccag	cctgcggccg	cgcattcttg	60
cgtctggcca	gccgcgagct	ctaagggctg	gccccgcccg	gtccgceccc	gcggtccct	120
gccaggctct	cgcgggcgcg	ctcggggtgg	ggcctcgcg	ctggcggaga	tgcggcggg	180
gctgcgcggt	ggtgatgcga	gcctgctggg	cggcgcgcgc	gggcagccgg	agccgcgcgc	240
cgcggcgctg	taatcggaca	ccaagagcgc	tcgcccccg	cctccggcca	ctttccattc	300
actccgaggt	gcttgattga	gcgacgcgga	gaagagctcc	gggtgcgcgc	gcactgcagc	360
gctgagattc	ctttacaaag	aaactcagag	gaccgggaag	aaagaatttc	acctttgcga	420
cgtgctagaa	aataaggctg	tctgggaaaa	ggactggaga	cacaagcgca	tccaaccccg	480
gtagcaaact	gatgactttt	ccgtgctgat	ttctttcaac	ctcggtattt	tcccttgat	540
attaacttgc	atatctgaag	aaatggcatt	ccggacaatt	tgcggtgttg	ttggagtatt	600
tatttgttct	atctgtgtga	aaggatcttc	ccagcccca	gcaagagttt	atttaacatt	660
tgatgaactt	cgagaaacca	agacctctga	atacttcagc	ctttcccacc	atcctttaga	720
ctacaggatt	ttattaatgg	atgaagatca	ggaccggata	tatgtgggaa	gcaaagatca	780
cattctttcc	ctgaatatta	acaatataag	tcaagaagct	ttgagtgttt	tctggccagc	840
atctacaatc	aaagttgaag	aatgcaaaat	ggctggcaaa	gatcccacac	acggctgtgg	900
gaactttgtc	cgtgtaattc	agactttcaa	tcgcacacat	ttgtatgtct	gtgggagtgg	960
cgctttcagt	cctgtctgta	cttacttgaa	cagagggagg	agatcagagg	accaagtttt	1020
catgattgac	tccaagtgtg	aatctggaaa	aggacgctgc	tctttcaacc	ccaacgtgaa	1080
cacgggtgtct	gttatgatca	atgaggagct	ttctcttgga	atgtatatag	atttcattgg	1140
gacagatgct	gctatttttc	gaagtttaac	caagaggaat	gcggtcagaa	ctgatcaaca	1200
taattccaaa	tggctaagtg	aacctatggt	tgtagatgca	catgtcatcc	cagatgggtac	1260
tgatccaaat	gatgctaagg	tgtacttctt	cttcaaagaa	aaactgactg	acaataacag	1320
gagcacgaaa	cagattcatt	ccatgattgc	tcgaatatgt	cctaatagaca	ctggtggact	1380
gcgtagcctt	gtcaacaagt	ggaccacttt	cttaaaggcg	aggctgggtgt	gctcggtaac	1440

- 94 -

agatgaagac	ggcccagaaa	cacactttga	tgaattagag	gatgtgtttc	tgctggaaac	1500
tgataacccg	aggacaacac	tagtgtatgg	cattttttaca	acatcaagct	cagtttttcaa	1560
aggatcagcc	gtgtgtgtgt	atcattttatc	tgatatacag	actgtgttta	atgggccttt	1620
tgcccacaaa	gaagggccca	atcatcagct	gatttcctat	cagggcagaa	ttccatatcc	1680
tgcacctgga	acttgtccag	gaggagcatt	tacaccaat	atgcgaacca	ccaaggagtt	1740
cccagatgat	gttgtcactt	ttattcggaa	ccatcctctc	atgtacaatt	ccatctaccc	1800
aatccacaaa	aggcctttga	ttgttcgtat	tggcactgac	tacaagtaca	caaagatagc	1860
tgtggatcga	gtgaacgctg	ctgatgggag	ataccatgtc	ctgtttctcg	gaacagatcg	1920
gggtactgtg	caaaaagtgg	ttgttcttcc	tactaacaac	tctgtcagtg	gcgagctcat	1980
tctggaggag	ctggaagtct	ttaagaatca	tgctcctata	acaacaatga	aaatttcatc	2040
taaaaagcaa	cagttgtatg	tgagttccaa	tgaaggggtt	tccaagtat	ctctgcaccg	2100
ctgccacatc	tatggtacag	cctgtgctga	ctgctgcctg	gcgcgggacc	cttattgcgc	2160
ctgggatggc	cattcctggt	ccagattcta	cccaactggg	aaacggagga	gccgaagaca	2220
agatgtgaga	catggaaacc	cactgactca	atgcagagga	tttaatctaa	aagcatacag	2280
aatgcagct	gaaattgtgc	agtatggagt	aaaaaataac	accacttttc	tggagtgtgc	2340
ccccaagtct	ccgcaggcat	ctatcaagtg	gctgttacag	aaagacaaag	acaggaggaa	2400
agaggttaag	ctgaatgaac	gaataatagc	cacttcacag	ggactcctga	tccgctctgt	2460
tcagggttct	gaccaaggac	tttatcactg	cattgctaca	gaaaatagtt	tcaagcagac	2520
catagccaag	atcaacttca	aagttttaga	ttcagaaatg	gtggctgttg	tgacggacaa	2580
atggtccccg	tggacctggg	ccagctctgt	gagggtttta	cccttccacc	cgaaggacat	2640
catgggggca	ttcagccact	cagaaatgca	gatgattaac	caatactgca	aagacactcg	2700
gcagcaacat	cagcagggag	atgaatcaca	gaaaatgaga	ggggactatg	gcaagttaaa	2760
ggccctcatc	aatagtcgga	aaagtagaaa	caggaggaat	cagttgccag	agtcataata	2820
ttttcttatg	tgggtcttat	gcttcatta	acaaatgctc	tgtcttcaat	gatcaaattt	2880
tgagcaaaga	aacttgtgct	ttaccaaggg	gaattactga	aaaaggatg	tactcctgaa	2940
gtgagtttta	cacgaactga	aatgagcatg	cattttcttg	tatgatagtg	actagcacta	3000
gacatgtcat	ggtcctcatg	gtgcatataa	atatatttaa	cttaaccag	attttattta	3060
tatctttatt	caccttttct	tcaaaatcga	tatggtggct	gcaaaactag	aattgttgca	3120
tccctcaatt	gaatgagggc	catatccctg	tggatattcct	ttcctgcttt	ggggcttttag	3180
aattctaatt	gtcagtgatt	ttgtatatga	aaacaagttc	caaattccaca	gcttttacgt	3240

agtaaaagtc ataaatgcat atgacagaat ggctatcaaa agaaatagaa aaggaagacg 3300
gcatttaaag ttgtataaaa acacgagtta ttcataaaga gaaaatgatg agtttttatg 3360
gttccaatga aatatcttcc ccttttttta agattgtaaa aataatcagt tactggtatc 3420
tgtcactgac ctttgtttcc ttattcagga agataaaaat cagtaacctt ccccatgaag 3480
atatttggtg ggagttatat cagtgaagca gtttggttta tattcttatg ttatcacctt 3540
ccaaacaaaa gcacttactt tttttggaag ttatttaatt tatttttagac tcaaagaata 3600
taatcttgca ctactcagtt attactgttt gttctcttat tccctagtct gtgtggcaaa 3660
ttaaacaata taagaaggaa aaatttgaag tattagactt ctaaataagg ggtgaaatca 3720
tcagaaagaa aaatcaaagt agaaactact aattttttta gaggaattta taacaaatat 3780
ggctagtttt caacttcagt actcaaattc aatgattctt ccttttatta aaaccagtct 3840
cagatatcat actgattttt aagtcaacac tatatatatt atgatctttt cagtgtgatg 3900
gcaagggtgct tggtatgtct agaaagtaag aaaacaatat gaggagacat tctgtctttc 3960
aaaaggtaat ggtacatacg ttcactggtc tctaagtgtt aaagtagtaa attttgtgat 4020
gaataaaata attatctcct aattgtatgt tagaataatt ttattagaat aatttcatac 4080
tgaaattatt ttctccaaat aaaaattaga tggaaaaatg tgaaaaaaat tattcatgct 4140
ctcatatata ttttaaaaac actacttttg cttttttatt taccttttaa gacattttca 4200
tgcttccagg taaaaacaga tattgtacca tgtacctaat ccaaatatca tataaacatt 4260
ttatttatag ttaataatct atgatgaagg taattaaagt agattatggc ctttttaagt 4320
attgcagtct aaaacttcaa aaactaaaat cattgtcaaa attaatatga ttattaatca 4380
gaatatcaga tatgattcac tatttaaact atgataaatt atgataatat atgaggaggc 4440
ctcgctatag caaaaatagt taaaatgctg acataacacc aaacttcatt ttttaaaaaa 4500
tctgttggtc caaatgtgta taatttttaa gtaatttcta aagcagttta ttataatggt 4560
ttgcctgctt aaaagggtata attaaacttc ttttctcttc tacattgaca cacagaaatg 4620
tgtcaatgta aagccaaaac catcttctgt gtttatggcc aatctattct caaagttaaa 4680
agtaaaattg tttcagagtc acagttccct ttatttcaca taagcccaaa ctgatagaca 4740
gtaacggtgt ttagttttat actatatatt tgctatttaa ttctttctat tttcacaatt 4800
attaaattgt gtacactttc attactttta aaaatgtaga aattcttcat gaacataact 4860
ctgctgaatg taaaagaaaa ttttttttca aaaatgctgt taatgtatac tactggtggt 4920
tgattggttt tatttttatgt agcttgacaa ttcagtgact taatatctat tccatttgta 4980

- 96 -

ttgtacataa aatTTTtctag aaatacactt ttttccaaag tgtaagtttg tgaatagatt 5040
 ttagcatgat gaaactgtca taatggtgaa tgttcaatct gtgtaagaaa acaaactaaa 5100
 tgtagttgtc aactaaaaat ttaattggat attgatgaaa tcattggcct ggcaaaaataa 5160
 aacatgttga attcccc 5177

<210> 59

<211> 2433

<212> DNA

<213> Homo sapiens

<400> 59

cagccgcggc ccatggagcc cgcgcggcccg gcccccggcc gcctcgggcc gctgctctgc 60
 ctgctgctcg ccgcgtcctg cgcctggtea ggagtggcgg gtgaggagga gctgcagggtg 120
 attcagcctg acaagtccgt atcagttgca gctggagagt cggccattct gcactgcact 180
 gtgacctccc tgatccctgt ggggcccata cagtggttca gaggagctgg accagcccgg 240
 gaattaatct acaatcaaaa agaaggccac ttcccccggg taacaactgt ttcagagtcc 300
 acaaagagag aaaacatgga cttttccata agcatcagta acatcacccc agcagatgcc 360
 ggcacctact actgtgtgaa gttccggaaa gggagccctg acacggagtt taagtctgga 420
 gcaggcactg agctgtctgt gcgtgccaaa ccctctgccc ccgtgggtatc gggccctgcg 480
 gcgagggcca cacctcagca cacagtgage ttcacctgcg agtcccacgg cttctcaccc 540
 agagacatca ccctgaaatg gttcaaaaat gggaatgagc tctcagactt ccagaccaac 600
 gtggaccocg taggagagag cgtgtcctac agcatccaca gcacagccaa ggtggtgctg 660
 acccgcgagg acgttcactc tcaagtcata tgcgaggtgg ccacggtcac cttgcagggg 720
 gacctcttc gtgggactgc caacttgtct gagaccatcc gagttccacc caccttggag 780
 gttactcaac agcccgtagg ggcagagaac caggtgaatg tcacctgcca ggtgaggaag 840
 ttctaccccc agagactaca gctgacctgg ttggagaatg gaaacgtgtc ccggacagaa 900
 acggcctcaa ccgttacaga gaacaaggat ggtacctaca actggatgag ctggctcctg 960
 gtgaatgtat ctgcccacag ggatgatgtg aagctcacct gccaggtgga gcatgacggg 1020
 cagccagcgg tcagcaaaag ccatgacctg aaggtctcag cccacccgaa ggagcagggc 1080
 tcaaataccg ccgtgagaa cactggatct aatgaacgga acatctatat tgtggtgggt 1140
 gtggtgtgca ccttgctggt ggcctactg atggcggcc tctacctgt ccgaatcaga 1200

- 97 -

cagaagaaag cccagggctc cacttcttct acaagggttg atgagcccga gaagaatgcc 1260
 agagaaataa cacaggacac aaatgatata acatatgcag acctgaacct gcccaagggg 1320
 aagaagcctg ctccccaggc tgcggagccc aacaaccaca cggagtatgc cagcattcag 1380
 accagcccgc agcccgcgtc ggaggacacc ctcacctatg ctgacctgga catggtccac 1440
 ctcaaccgga cccccaagca gcgggcccc aagcctgagc cgtccttctc agagtacgcc 1500
 agcgtccagg tcccaggagaa gtgaatggga ccgtgggttg ctctagcacc catctctacg 1560
 cgctttcttg tcccacaggg agccgccgtg atgagcacag ccaaccagc tcccggaggg 1620
 ctggggcggt gcaggctctg ggaccaggg gccagggtgg ctcttctctc cccaccctc 1680
 cttggtctc cagcacttcc tgggcagcca cggccccctc cccaacatt gccacacacc 1740
 tggaggctga cgttgccaaa ccagccaggg aaccaacctg ggaagtggcc agaactgcct 1800
 ggggtccaag aactcttggt cctccgtcca tcaccatgtg ggttttgaag accctcgact 1860
 gcctccccga tgctccgaag cctgatcttc cagggtgggg aggagaaaat cccacctccc 1920
 ctgacctcca ccacctccac caccaccacc accaccacca ccaccactac caccaccacc 1980
 caactggggc tagagtgggg aagatttccc ctttagatca aactgcccct tccatggaaa 2040
 agctggaaaa aaactctgga acccatatcc aggttggtg aggttgctgc caacagtcct 2100
 ggctcccc atccctaggg aaagagccat gagtcctgga ggaggagagg accctccca 2160
 aaggactgga agcaaaaccc tctgcttctc tgggtccctc caagactccc tggggcccaa 2220
 ctgtgttgct ccaccggac ccatctctcc cttctagacc tgagcttgcc cctccagcta 2280
 gcactaagca acatctcgct gtaagcgct gtaaattact gtgaaatgtg aaacgtgcaa 2340
 tcttgaaact gaggtgttag aaaacttgat ctgtggtgtt ttgttttggt ttttttctta 2400
 aaacaacagc aacgtgaaaa aaaaaaaaaa aaa 2433

<210> 60

<211> 2181

<212> DNA

<213> Homo sapiens

<400> 60

ctgcttgggg acctccttct agccttaaata ttcagctcat caccttcacc tgccttggtc 60
 atggctctgc tattctcctt gatccttgcc atttgacca gacctggatt cctagcgtct 120

ccatctggag	tgcggtggt	ggggggcctc	caccgctgtg	aagggcggt	ggaggtggaa	180
cagaaaggcc	agtggggcac	cgtgtgtgat	gacggctggg	acattaagga	cgtggctgtg	240
ttgtgccggg	agctgggctg	tggagctgcc	agcggaaccc	ctagtggat	tttgtatgag	300
ccaccagcag	aaaaagagca	aaaggtcctc	atccaatcag	tcagttgcac	aggaacagaa	360
gatacattgg	ctcagtgtga	gcaagaagaa	gtttatgatt	gttcacatga	tgaagatgct	420
ggggcatcgt	gtgagaaccc	agagagctct	ttctccccag	tcccagaggg	tgtcaggctg	480
gctgacggcc	ctgggcattg	caagggacgc	gtggaagtga	agcaccagaa	ccagtggat	540
accgtgtgcc	agacaggctg	gagcctccgg	gccgcaaagg	tgggtgtgcc	gcagctggga	600
tgtgggaggg	ctgtactgac	tcaaaaacgc	tgcaacaagc	atgcctatgg	ccgaaaaccc	660
atctggctga	gccagatgtc	atgctcagga	cgagaagcaa	cccttcagga	ttgcccttct	720
gggccttggg	ggaagaacac	ctgcaaccat	gatgaagaca	cgtgggtcga	atgtgaagat	780
ccctttgact	tgagactagt	aggaggagac	aacctctgct	ctgggcgact	ggaggtgctg	840
cacaagggcg	tatggggctc	tgtctgtgat	gacaactggg	gagaaaagga	ggaccagggtg	900
gtatgcaagc	aactgggctg	tgggaagtcc	ctctctccct	ccttcagaga	ccggaaatgc	960
tatggccctg	gggttggccg	catctggctg	gataatgttc	gttgctcagg	ggaggagcag	1020
tccctggagc	agtgccagca	cagattttgg	gggtttcacg	actgcacca	ccaggaagat	1080
gtggctgtca	tctgctcagg	atagtatcct	ggtgttgctt	gacctggccc	ccctggcccc	1140
gcctgccctc	tgcttggtct	cctgagccct	gattatcctc	atactcattc	tggggctcag	1200
gcttgagcca	ctactccctc	atcccctcag	gagtctgaac	actgggctta	tgcttactc	1260
tcagggacaa	gcagccccct	ttgctgcctg	tagatgtgag	ctgttgagtt	ccctcttgct	1320
ggggaagatg	agcttccatg	tatcctgtgc	tcaaccctga	ccctttgaca	ctggttctgg	1380
cccttcctgc	cttttctcaa	gctgcctgga	atcctcaaac	ctgtcacttt	ggtcagatgt	1440
gcagaccatt	actaaggctc	atgtctgcaa	acattactaa	tctaggtcct	attactaatc	1500
tatgtctgca	aacattaaag	gaatgaaaca	atgaaaggaa	catttgaaag	aaaatgtggg	1560
tagacaattt	cttgcaactt	gggggaaagt	ttagaattct	tttgattgga	ctactttttt	1620
ttttttcctc	aagcttcagg	tgaccacaat	agcaacacct	ccctattctg	ttattttctta	1680
gtgtaggtag	acaattcttt	caggagcaga	gcagcgtcct	ataatcctag	accttttcat	1740
gacgtgtaaa	aatgatgtt	tcatcctctg	attgccccaa	taaaaatctt	tgttgtecat	1800
ccctatacaa	cctgccaaca	tggttgacat	ttaatgagag	gaatgtcaaa	aatacatttt	1860
actttattca	aagaaaaata	tattggttac	tgggaaaagg	tcaagaaaga	ggcagaaaga	1920

- 99 -

gatcagggag ggctaaagtt gtgtcttatg ccaageggaa gtggaaaata tcacttttca 1980
ctttatcaac tgagactttg gggcctgtaa gcttgaggca agacagaaat aagagaatca 2040
agacttgatt gtaaaaattg acaactttag attctgaggc taggctgagt acttattata 2100
cggctacatt tacacattta cacttatcta ataaatcaga tttcacagtc tcaaaaaaaaa 2160
aaaaagaaaa aaaaaaaaaa a 2181

<210> 61

<211> 980

<212> DNA

<213> Homo sapiens

<400> 61

gctttcttgg gaagatggcg gctgtgtcgg tgtatgctcc accagttgga ggcttctctt 60
ttgataactg ccgcaggaat gccgtcttgg aagccgattt tgcaaagagg ggatacaagc 120
ttccaaaggt ccggaaaact ggcacgacca tcgctggggg ggtctataag gatggcatag 180
ttcttggagc agatacaaga gcaactgaag ggatggttgt tgctgacaag aactgttcaa 240
aaatacactt catatctcct aatatttatt gttgtggtgc tgggacagct gcagacacag 300
acatgacaac ccagctcatt tcttccaacc tggagctcca ctccctctcc actggccgctc 360
tccccagagt tgtgacagcc aatcggatgc tgaagcagat gcttttcagg tatcaagggt 420
acattggtgc agccctagtt ttaggggggag tagatgttac tggacctcac ctctacagca 480
tctatcctca tggatcaact gataagttgc cttatgtcac catgggttct ggctccttgg 540
cagcaatggc tgtatttgaa gataagttta ggccagacat ggaggaggag gaagccaaga 600
atctggtgag cgaagccatc gcagctggca tcttcaacga cctgggctcc ggaagcaaca 660
ttgacctctg cgtcatcagc aagaacaagc tggattttct ccgccatac acagtgccca 720
acaagaaggg gaccaggctt ggccgggtaca ggtgtgagaa agggactact gcagtcctca 780
ctgagaaaaat cactcctctg gagattgagg tgctggaaga aacagtccaa acaatggaca 840
cttcctgaat ggcatcagtg ggtggctggc cgcggttctg gaagggtggtg agcattgagg 900
cccagtaaga cactcatgtg gctagtgttt gccgaatgaa actcaactca ataaaaaaca 960
aaaaccaaat tgggcagctg 980

- 100 -

<210> 62

<211> 3727

<212> DNA

<213> Homo sapiens

<400> 62

gtcgcggtgt gctaagcgag gagtccgagt gtgtgagctt gagagccgcg cgctagagcg	60
accgcggcgag ggatggcggc caccgggacc gcggccgcgc cagccacggg caggctcctg	120
cttctgctgc tgggtggggt cacggcgcct gccttggcgc tggccggcta catcgaggct	180
cttgcagcca atgccggaac aggatttgct gttgctgagc ctcaaategc aatgttttgt	240
gggaagttaa atatgcatgt gaacattcag actgggaaat gggaacctga tccaacaggc	300
accaagagct gctttgaaac aaaagaagaa gttcttcagt actgtcagga gatgtatcca	360
gagctacaga tcacaaatgt gatggaggca aaccagcggg ttagtattga caactggtgc	420
cggagggaca aaaagcaatg caagagtcgc tttgttacac ctttcaagtg tctcgtgggt	480
gaatttgtaa gtgatgtcct gctagttcca gaaaagtgcc agtttttcca caaagagcgg	540
atggagggtgt gtgagaatca ccagcactgg cacacggtag tcaaagaggc atgtctgact	600
cagggaatga ccttatatag ctacggcatg ctgctcccat gtggggtaga ccagttccat	660
ggcactgaat atgtgtgctg ccctcagaca aagattattg gatctgtgtc aaaagaagag	720
gaagaggaag atgaagagga agaggaagag gaagatgaag aggaagacta tgatgtttat	780
aaaagtgaat ttctactga agcagatctg gaagacttca cagaagcagc tgtggatgag	840
gatgatgagg atgaggaaga aggggaggaa gtgggtggagg accgagatta ctactatgac	900
accttcaaag gagatgacta caatgaggag aatcctactg aaccggcag cgacggcacc	960
atgtcagaca aggaaattac tcatgatgtc aaagctgtct gctcccagga ggcgatgacg	1020
gggccctgcc gggccgtgat gcctcgttgg tacttcgacc tctccaaggg aaagtgcgtg	1080
cgctttatat atgggtggctg cggcggcaac aggaacaatt ttgagtctga ggattattgt	1140
atggctgtgt gtaaagcgat gattcctcca actcctctgc caaccaatga tgttgatgtg	1200
tatttcgaga cctctgcaga tgataatgag catgctcgct tccagaaggc taaggagcag	1260
ctggagattc ggcaccgcaa ccgaatggac agggtaaaga aggaatggga agaggcagag	1320
cttcaagcta agaacctccc caaagcagag aggcagactc tgattcagca cttccaagcc	1380
atgggttaaag ctttagagaa ggaagcagcc agtgagaagc agcagctggt ggagaccac	1440

- 101 -

ctggcccgag	tggaagctat	gctgaatgac	cgccgtcgga	tggtctctgga	gaactacctg	1500
gctgccttgc	agtctgaccc	gccacggcct	catcgcatte	tccaggcctt	acggcgttat	1560
gtccgtgctg	agaacaaaga	tcgcttacat	accatccgtc	attaccagca	tgtgttggct	1620
gttgacccag	aaaaggcggc	ccagatgaaa	tcccaggtga	tgacacatct	ccacgtgatt	1680
gaagaaagga	ggaaccaaag	cctctctctg	ctctacaaag	taccttatgt	agcccaagaa	1740
attcaagagg	aaattgatga	gctccttcag	gagcagcgtg	cagatatgga	ccagttcact	1800
gcctcaatct	cagagacccc	tgtggacgtc	cgggtgagct	ctgaggagag	tgaggagatc	1860
ccaccgttcc	acoccttcca	ccccttcca	gccctacctg	agaacgaaga	cactcagccg	1920
gagttgtacc	acccaatgaa	aaaaggatct	ggagtgggag	agcaggatgg	gggactgatc	1980
ggtgccgaag	agaaagtgat	taacagtaag	aataaagtgg	atgaaaacat	ggtcattgac	2040
gagactctgg	atgttaagga	aatgattttc	aatgccgaga	gagttggagg	cctcgaggaa	2100
gagcgggaat	ccgtgggccc	actgcgggag	gacttcagtc	tgagtagcag	tgctctcatt	2160
ggcctgctgg	tcatcgcagt	ggccattgcc	acggtcacgc	tcacagcct	ggtgatgctg	2220
aggaagaggc	agtatggcac	catcagccac	gggatcgtgg	aggttgatcc	aatgctcacc	2280
ccagaagagc	gtcacctgaa	caagatgcag	aaccatggct	atgagaaccc	cacctacaaa	2340
tacctggagc	agatgcagat	ttaggtggca	gggagcgagg	cagccctggc	ggagggatgc	2400
aggtgggccc	gaagatccca	cgattccgat	cgactgccaa	gcagcagccg	ctgccagggg	2460
ctgcgtctga	catcctgacc	tcctggactg	taggactata	taaagtacta	ctgtagaact	2520
gcaatttcca	ttctttttaa	tgggtgaaaa	atggtaatat	aacaatatat	gatataataa	2580
ccttaaataa	aaaaaatgat	ctattgcaga	tatttgatgt	agttttcttt	tttaaattaa	2640
tcagaaaccc	cacttccatt	gtattgtctg	acacatgctc	tcaatatata	ataaatggga	2700
aatgtcgatt	ttcaataata	gacttatatg	caggctgtcg	ttccggttat	gttgtgtaag	2760
tcaactcttc	agcctcattc	actgtcctgg	cttttattta	aagaaaaaaa	aggcagtatt	2820
ccctttttta	atgagctttc	aggaagtgtc	tgagaaatgg	ggtggaatag	ggaactgtaa	2880
tggccactga	agcacgtgag	agaccctcgc	aaaatgatgt	gaaaggacca	gtttcttgaa	2940
gtccagtgtt	tccacggctg	gatacctgtg	tgtctccata	aaagtcctgt	caccaaggac	3000
gttaaaggca	ttttattoca	gcgtcttcta	gagagcttag	tgtatacaga	tgagggtgtc	3060
cgctgctgct	ttccttcgga	atccagtgtc	tccacagaga	ttagcctgta	gcttatattt	3120
gacattcttc	actgtctgtt	gtttacctac	cgtagctttt	taccgttcac	ttccccttcc	3180
aactatgtcc	agatgtgcag	gctcctcctc	tctggacttt	ctccaaaggc	actgaccctc	3240

- 102 -

ggcctctact ttgtcccctc acctccaccc cctcctgtca ccggccttgt gacattcact 3300
cagagaagac cacaccaagg agggggccgcg gctggcccag gagagaacac ggggagggtt 3360
gtttgtgtga aaggaaagta gtccaggctg tcctgaaac tgagtctgtg gacactgtgg 3420
aaagctttga acaattgtgt tttcgtcaca ggagtctttg taatgcttgt acagttgatg 3480
tcgatgetca ctgcttctgc tttttcttct tttttatttt aaaaaatctg aaggttctgg 3540
taacctgtgg tgtattttta ttttcctgtg actgtttttg ttttgttttt ttcttttttc 3600
ctccccctta gccctattca tgtctctacc cactatgcac agattaaact tcacctacaa 3660
actccttaat atgatctgtg gagaatgtac acagtttaaa cacatcaata aatactttaa 3720
cttccaa 3727

<210> 63

<211> 2143

<212> DNA

<213> Homo sapiens

<400> 63

aaaacattag gctcttgacg gaagcattgc ttgttaggag ccatcctgtg ctttcagggtg 60
tcacagatta gcatgggggtt ggagggtggg agacagcate ctgaagagca ggggtaggtg 120
tggttttgcc tggggctgtg gcagagagga gagacatgca gttatcaaaa gagtcagctg 180
cactgtcttt ttagctttgc cctgtggaca ctggaactca gctatttgga gtttccaaca 240
tctctcacat caagtccaag gagaaccttt cccttagttt cctcagctgc agaatgggct 300
gctgacttct cagggacttt gagggataa ctttcatttc attcaccag cagtgcctc 360
atgtttactg ttttcaatga gtaacagttg tctccattag tttgtgtttg ttgttttgta 420
attctgcctt ttttttctct ctctctctat ccctactcca aacagggtacc ctgtttgctt 480
gtattgcttt cttagaaaca cttggaggag tcaactgcagt ttctactttt aatggaattt 540
actcagccac tggtgcttgg taccctggct tcaacttctc gctgtctgct ggtctgttac 600
tacttcagc catcagtcta tgtgttgta agtgtaaccag ctggaatgag ggaagctatg 660
aacttcttat acaagaagaa tccagtgaag atgctccaga cagggtgactg tgatttaaac 720
aaacaaaaaa aatctatgaa tgcacatctc atataccatg acttctgaag actataaatg 780
aattccacaa tcagtgtctc actgagaacc aattttacct atcttttctt ctaaactgaa 840

- 103 -

cagtcagaga gacagctcct ggcttttagct tcttggtgga ccacgcactt tgagcacttt 900
 gtgcgtatca tgcaatatac ttgcaataca cagaacaaat ttcaaatacg cctcactttt 960
 agacttagaa gagaaacatt aaaacttaag ggtgtaagga gggatcaaga aacttgataa 1020
 ggtcaaaagc aataatctct ctgacatatt ccaggctctt acactgagac caaagagaaa 1080
 tctttacctc agtttcttca tcagcagaat gggtttctgg cttctctcag ggataatttt 1140
 gaaggcataa tgaaaattat gatgaatcac tcattggtag gaaaataatg atataagttt 1200
 cgaatatgta taattttacc tatacttggg aatgctttgt tttatagagc ctgttaagct 1260
 gctattgata gtoggagctt atatactgtg acttctgaag actatacatg aattccacaa 1320
 tcagtgcttt gttgatacaa aatccttaaa agggaggcac ttttaaagaa tatgtatttt 1380
 tcacttttct taatatgttt catcggtgac aggcattgata atatttctat atgtaatggg 1440
 taattgggaa aaaatagatg ataaataaaa ttgctctaaa gaagttaaaa aactgaatga 1500
 acagctaata ctggtataaa gtaactaatg tttggagcca acatttggtc cttgtgtcag 1560
 caaaaggata ttcacattcc atgatccctg gctgagaatt ctgcctctag tctttcttac 1620
 ccagctgttg tctatccttg ttcaattata aatactgcta agggcatttt taaaatacga 1680
 tcttgtaactc cttaaatttg aatccgtcgg cacgggcact cataggaaaa tgatcaaaca 1740
 agcaagccag tcatgatttg actccttccc atctcatttc ttactgcctt acgctcatcc 1800
 tgagggtccac cttggtctct aaaaacacca tgtgttctca tgcctccatg tcttttcaca 1860
 cactgttcca tttgctcttc ctcccacatt acattgaaac tttcaagcct cagtcgaaac 1920
 attgcttctt ctggatagca gccttcttga catccctcct cactccccag tccctacagg 1980
 gcttccatag ctctttatgt gcacttcgat ccagcattt tccatcgact tgtaattggt 2040
 tctgctacct gacaatcatc gccttgagta ctgggacaac ctttgattac tcattatatc 2100
 ctcaataaat atttgttgaa ctaaaaaaaaa aaaaaaaaaa aaa 2143

<210> 64

<211> 1806

<212> DNA

<213> Homo sapiens

<400> 64

gccgctcgct eggetceget ccctggctcg gctccctgcc tccgcgtcgc agcccccgcc 60

gtagccgcct ccgagccgcg cgcacatcc tctgagaaga tggtgtgcc acccacgtat 120

- 104 -

gccgatcttg gcaaattctgc cagggatgtc ttcaccaagg gctatggatt tggcttaata	180
aagcttgatt tgaaaacaaa atctgagaat ggattggaat ttacaagctc aggctcagcc	240
aacactgaga ccaccaaagt gacgggcagt ctggaaacca agtacagatg gactgagtac	300
ggcctgacgt ttacagagaa atggaatacc gacaatacac taggcaccga gattactgtg	360
gaagatcagc ttgcacgtgg actgaagctg accttcgatt catccttctc acctaacact	420
gggaaaaaaa atgctaaaat caagacaggg tacaagcggg agcacattaa cctgggctgc	480
gacatggatt tcgacattgc tgggccttcc atccggggtg ctctgggtgct aggttacgag	540
ggctggctgg ccggctacca gatgaatddd gagactgcaa aatcccagat gaccagagc	600
aactttgcag ttggctacaa gactgatgaa ttccagcttc aactaatgt gaatgacggg	660
acagagtttg gcggctccat ttaccagaaa gtgaacaaga agttggagac cgctgtcaat	720
cttgccctgga cagcaggaaa cagtaacacg cgcttcggaa tagcagccaa gtatcagatt	780
gaccctgacg cctgcttctc ggctaaagtg aacaactcca gcctgatagg tttaggatac	840
actcagactc taaagccagg tattaaactg aactgtcag ctcttctgga tggcaagaac	900
gtcaatgctg gtggccacaa gcttgggtcta ggactggaat ttcaagcata aatgaatact	960
gtacaattgt ttaattttta actatttttg agcatagcta ccttcagaat ttagtgtatc	1020
ttttaatgtt gtatgtctgg gatgcaagta ttgctaaata tgtagccct ccagggttaa	1080
gttgattcag ctttaagatg ttacccttcc agaggtagag aagaaacct tttccaaaa	1140
aggtcctttc agtggttagac tcggggagaa cttggtggcc cctttgagat gccaggtttc	1200
ttttttatct agaaatggct gcaagtggaa gcggataata tgtaggcact ttgtaaattc	1260
atattgagta aatgaatgaa attgtgattt cctgagaatc gaaccttggg tccctaacc	1320
taattgatga gaggctcgct gcttgatggg gtgtacaaac tcacctgaat gggacttttt	1380
tagacagatc ttcattgacct gttcccaccc cagttcatca tcattctctt tacaccaaaa	1440
ggtctgcagg gtgtggtaac tgttttcttt gtgccatttt ggggtggaga aggtggatgt	1500
gatgaagcca ataattcagg acttattcct tcttggtgtg tgtttttttt tggcccttgc	1560
accagagtat gaaatagctt ccaggagctc cagctataag cttggaagtg tctgtgtgat	1620
tgtaatcaca tgggtgacaac actcagaatc taaattggac ttctgttgta ttctcaccac	1680
tcaatttggt ttttagcagt ttaatgggta catttttagag tcttccattt tggttgaatt	1740
agatcctccc cttcaaatgc tgtaattaac aacacttaaa aaacttgaat aaaatattga	1800
aacctc	1806

- 105 -

<210> 65

<211> 2115

<212> DNA

<213> Homo sapiens

<400> 65

ctcgccecgte	cggcgcacgc	tccgcctccg	tcagttggct	cogctgtcgg	gtgcgcggcg	60
tggagcggca	gccggtctgg	acgcgcggcc	ggggctgggg	gctgggagcg	cggcgcgcaa	120
gatctccccg	cgcgagagcg	gcccctgcca	ccgggcgagg	cctgcgcgcg	gatggcagag	180
atgggcagta	aaggggtgac	ggcgggaaag	atcgccagca	acgtgcagaa	gaagctcacc	240
cgcgcgcagg	agaaggttct	ccagaagctg	gggaaggcag	atgagaccaa	ggatgagcag	300
tttgagcagt	gcgtccagaa	tttcaacaag	cagctgacgg	agggcacccg	gctgcagaag	360
gatctccgga	cctacctggc	ctccgtcaaa	gccatgcacg	aggcttccaa	gaagctgaat	420
gagtgtctgc	aggaggtgta	tgagcccgat	tggcccggca	gggatgaggc	aaacaagatc	480
gcagagaaca	acgacctgct	gtggatggat	taccaccaga	agctggtgga	ccaggcgctg	540
ctgaccatgg	acacgtacct	gggccagttc	cccgacatca	agtcacgcac	tgccaagcgg	600
gggcgcaagc	tggtggacta	cgacagtgcc	cggcaccact	acgagtcctt	tcaaactgcc	660
aaaaagaagg	atgaagccaa	aattgccaa	gccgaggagg	agctcatcaa	agcccagaag	720
gtgtttgagg	agatgaatgt	ggatctgcag	gaggagctgc	cgtccctgtg	gaacagccgc	780
gtaggtttct	acgtcaacac	gttccagagc	atcgcgggcc	tggaggaaaa	cttccacaag	840
gagatgagca	agctcaacca	gaacctcaat	gatgtgctgg	tcggcctgga	gaagcaacac	900
gggagcaaca	ccttcacggt	caaggcccag	cccagtgaca	acgcgcctgc	aaaagggaac	960
aagagccctt	cgcctccaga	tggctccctt	gccgccaccc	ccgagatcag	agtcaaccac	1020
gagccagagc	cggcggggcg	ggccacgccc	ggggccaccc	tccccaaagtc	cccatctcag	1080
ctcoggaaag	gcccaccagt	ccctccgcct	cccaaacaca	ccccgtccaa	ggaagtcaag	1140
caggagcaga	tcctcagcct	gtttgaggac	acgtttgtcc	ctgagatcag	cgtgaccacc	1200
ccctcccagc	cagcagaggc	ctcggagggtg	gcgggtggga	cccaacctgc	ggctggagcc	1260
caggagccag	gggagacggc	ggcaagtga	gcagcctcca	gctctcttcc	tgctgtcgtg	1320
gtggagacct	tcccagcaac	tgtgaatggc	accgtggagg	gcggcagtg	ggccggggcg	1380
ttggacctgc	ccccagggtt	catgttcaag	gtacaggccc	agcacgacta	cacggccact	1440

- 106 -

gacacagacg agctgcagct caaggctggt gatgtggtgc tggatgatccc cttccagaac 1500
 cctgaagagc aggatgaagg ctggctcatg ggcgtgaagg agagcgactg gaaccagcac 1560
 aaggagctgg agaagtgcg tggcgtcttc cccgagaact tcactgagag ggtcccatga 1620
 cggcggggcc caggcagcct ccgggcgtgt gaagaacacc tcctcccgaa aaatgtgtgg 1680
 ttcttttttt tgttttgttt tcgtttttca tcttttgaag agcaaaggga aatcaagagg 1740
 agacccccag gcagaggggc gttctcccaa agattaggte gttttccaaa gagccgcgtc 1800
 ccggcaagtc cggcgggaatt caccagtgtt cctgaagctg ctgtgtcctc tagttgagtt 1860
 tctggcgccc ctgcctgtgc ccgcatgtgt gcctggccgc agggcggggc tgggggctgc 1920
 cgagccacca tgcttgctg aagcttcggc cgcgccaccc gggcaagggt cctcttttcc 1980
 tggcagctgc tgtgggtggg gccagacac cagcctagcc tggctctgcc ccgcagacgg 2040
 tctgtgtgct gtttgaaaat aaatcttagt gttcaaaaca aaatgaaaca aaaaaaaaaat 2100
 gataaaaact ttcag 2115

<210> 66

<211> 5052

<212> DNA

<213> Homo sapiens

<400> 66

cggcgctttt ccttcggact aaggagccg tcgaagagcg ctcgccaaag gccagccgtt 60
 tctccctacg gtgcgcgcgc tcctcctgca gccgcccgta ggtagcgggc cgttttcttc 120
 acctgtccct gacaggcgcc ctcagggagc cgcgggtccgc gatgtcaagc gaggaaagct 180
 accgggcat cctgcgttac ctgacgaacg agcgcgagcc gtatgcgccg ggcaccgagg 240
 gcaatgtcaa gcgtaaaatc cgaaaagctg ccgcctgcta cgtggtgcgc ggcgggactc 300
 tgtattacca gcggcggcag cggcaccgca agaccttcgc ggagctggag gtggtgctgc 360
 agccggagcg acgcggggac ctcatcgagg cggcgcacct ggggtcccggc ggcactcacc 420
 acacccggca tcagacctgg cactacttgt ccaagacgta ctggtggcga ggtatattga 480
 agcaagtcaa agattacatt aaacagtgtg gcaaagtcca ggagaaacta gatcgatccc 540
 gtccaatatc agatgtttca gaaatgttgg aagaattggg actagacctt gaatctggag 600
 aagaaagtaa tgaatcggaa gatgacctga gcaactttac ttcattctca actacagcat 660

- 107 -

ccaagcctgc aaaaaagaag ccagtatcca aacatgaact tgtgtttgtt gacaccaaag	720
gagtggtaaa acgttcttct ccaaaacatt gtcaggctgt cttaaaacag ctgaacgaac	780
agagactttc caaccagttc tgtgatgtta ctttgttaat tgaaggagaa gagtacaaag	840
ctcataaate tgttttgtca gcaaatagcg agtattttcg agatcttttt attgagaaag	900
gagctgtttc cagtcattgag gctgtggtgg atctttctgg tttttgtaag gccagcttcc	960
ttcctttact ggaatttgcc tataactctg tactaagttt tgatttctgt agcatggctg	1020
atgtagccat cttagctcgt catcttttca tgtcagaagt cttagagatt tgtgaaagtg	1080
tacataagct aatggaagag aagcagctaa cagtatataa gaagggcgaa gtacaaacag	1140
ttgcatccac ccaggactta cgagtacaga atggaggtag agcacctcct gttgctagca	1200
gtgagggaac cacaacaagt ttacctactg aacttgggga ttgtgaaatt gtactactgg	1260
taaatggaga attgccagaa gctgagcaga atggagaggt aggacgacag cctgagcccc	1320
aggtttcttc agaggctgaa tctgccctgt catcagtagg atgtatagct gattcccatc	1380
ctgaaatgga gtctgttgat ttaataacaa aaaacaacca gacagaacta gaaacttcaa	1440
acaacagaga aaataacaca gtttctaata tacaccctaa actttcaaaa gagaatgtaa	1500
ttagtagctc gccagaggat agtggtatgg gaaatgatat atcagctgag gatatttgtg	1560
ccgaagacat tccaaaacat aggcagaaag ttgaccaacc tttaaaagat caggaaaatc	1620
tagttgcac aacagcaaag acaaactttg gccctgatga tgatacttat agaagcaggc	1680
ttcgacaacg ttctgttaat gaaggggcat atattcgact acacaaggga atggagaaaa	1740
agctgcagaa acggaaagcc gttcccaagt cagcagttca acaggtggct cagaagttag	1800
ttcaaagagg aaaaaagatg aaacagccaa aaagagatgc taaagagaac acagaagaag	1860
catctcataa atgtggggaa tgtggaatgg tttttcagag acgatacgcc cttataatgc	1920
acaaactgaa acatgaaaga gctagagatt acaaatgtcc atttgttaaa aaacagtttc	1980
agtacagtgc ctctttgcga gcacatctta ttcgtcatac cagaaaagat gcacctctt	2040
catcctcgtc caattccacg tctaatagaag catcggaac atcatctgag aagggcagaa	2100
ccaagcggga atttatatgt tccatatgtg gaagaacatt acctaaatta tattctctcc	2160
gaatacatat gttaaagcac acaggtgtaa agccacatgc atgccaggtc tgtggaaaga	2220
cttttatcta taagcatggg ctaaaattac atcagagtct tcatcaatca cagaagcagt	2280
tccagtgtga actgtgtgtt aagtcatttg ttaccaaacg gagtcttcaa gaacatatga	2340
gtattcacac aggagagtcc aagtaccttt gctcagtttg tggaaagtct tttcataggg	2400
gctctggact cagcaagcac ttcaagaaac accaaccaaa gcctgagggt cgaggctatc	2460

- 108 -

attgtactca atgtgaaaaa agtttctttg aagctagaga tcttcgccag cacatgaaca 2520
aacatcttgg tgtgaagcca ttccagtgcc aattttgtga taagtgctat agttggaaga 2580
aagattggta ttcccatgtg aagtctcatt ctgtcactga gccttatagg tgtaatatat 2640
gtggcaaaga attttatgaa aaagctttgt tcagaaggca tgtaaagaaa gctacccatg 2700
ggaagaaagg aagagcaaag caaaacctgg aacgggtgtg tgaaaaatgt ggaagaaaat 2760
tcactcagct aagagagtat aggagacaca tgaacaacca tgaaggagtt aagccatttg 2820
agtgcctaac atgtggagta gcttgggctg atgcccgatc tctaaaacgc catgtcagaa 2880
cacatactgg tgaacggccc tatgtctgtc ctgtatgtag cgaagcctac atagatgctc 2940
gaacactccg taaacatatg actaaattcc acagagacta tgtgccttgc aaaattatgc 3000
tggaanaaga cacccttcag tttcataacc aaggaactca agtggcacat gctgttagca 3060
tcttaacagc aggcattgcag gaacaagaaa gcagtgggtcc tcaagaactt gagactgtgg 3120
tagtgacagg agaaactatg gaagctctgg aagctgttgc agctactgaa gagtatccat 3180
cggtatctac actttctgac caaagtatta tgcaagtggc taattatgta ttagcacaac 3240
agcaaggaca gaagctatct gaagttgcag aagctattca aactgttaaa gtagaggtag 3300
cacatatctc aggaggagaa tgagtatggt aatgaagata aaaagaagtg acatctcttg 3360
tacactgaac tcacagaaca tttgtttaca attctgtgtg actgtctgct tggagtttac 3420
atatcaaagt tctgggctgt ttggtaacgt aacgtttcca aacattttgt ctggccaatg 3480
ggttctatag aaaagaccgt ttagtgtaga gaaattgaaa acagatctat taggttggtg 3540
caattgcttt tgcaccaacc taatatttga tggcagtggc ttatcatgat atacctttta 3600
tgaattaatg tttataaatg actgtactga atttaaaacc gtacagtttc atttgcattt 3660
tgacattact ttattataca ttttgcattt aaaaggctgc accagtgggc ttttcttctg 3720
ttttattctc aaaatataga gattctgtga tttatttgcc ctgtttatgg attaaaaaga 3780
aaattctaata ataaagcatt tcaataggat gcataggtat attacgtttt ttaaagtctt 3840
tagatctgtg attcttgact tactatttat tttatccctt ttaagtcag ggatgcttta 3900
ttctatttta aagcacttat gagttacatg ttgtaatcaa gtttgcacaa tatatttate 3960
tatatgagga acccataaat gaatagctaa tttttaaaat gccattaaaa tgcataaat 4020
gcttattaaa accttactat actatttctt caagggaag taaattgacc atgagaaaag 4080
aacacagtta ttaaactctg ttgacaggaa aattctcctt gataacatag gacaattaat 4140
ggaaaaaaaa attctcatta tttgcaaaga atgaacaagt taatgaacaa acaaactaga 4200

- 109 -

```

tttggtatgt tttcagcttt tgtatcatgt ttaattgttt aatttggttg aaaaactgca 4260
gttgagaaat cagatagcaa tatagacatt cacagcagct ctgtggatac catgtaattg 4320
tcaggtaatt tcagaatggt gaaaattatt cagtgcagcc ctcatagtat catacttgaa 4380
gaaattgatt accgttccac taaattgttg aagataaatt atttttaaag gttatgaaaa 4440
ctaagttata ttaattcata tgtttgattt ttaaatccca cctcctcaag ctatccaatt 4500
ttctgacttt gaaaataacc atgagagatg ccacatttct ctctgggaaa ctaccactca 4560
aagaataatt gttaaaaatt aagcttttag gtattagaag ctgttataaa gtataaaatt 4620
aagatataag cagatcacat gtaaatcatt cctaaagcac aagaaaagaa tgtgccttga 4680
tgtacatata ttactaagtt gcctctccca gtttacttta aaaatggctt taaggataaa 4740
gaataaatgt gatagctgtg catgcattat atatttgcac ttgcaaattt cccattgttt 4800
taacagctgt gtggctgact ttcaatttta agacgtgaat tgacatacag ccataaactt 4860
tataatggct gctcatttat cttatcttcc agttagtggg aaaacatttc aacctgacta 4920
aaatttgga ttgtgtcttt ttatgttcca tcctctgttg ttactagatt tagtttaaaa 4980
attgtgtatg accattaatg tatgtcataa acatgtaaat aaaagatggt gaatcttggt 5040
gaaagcgcgg cc 5052

```

<210> 67

<211> 639

<212> DNA

<213> Homo sapiens

<400> 67

```

ggacggaggg cacgagagaa ggagacgctg cagaaagagg cctccagctt ggtctgtctc 60
ccacctctac cagatctgct gagctatgag ccaaaccagg gatttacagg gaggaaaagc 120
tttcggactg ctgaaggccc agcaggaaga gaggctggat gagatcaaca agcaattcct 180
acacgatccc aaatatagca gtgatgagga tctgccctcc aaactggaag gcttcaaaga 240
gaaatacatg gagtttgacc ttaatggaaa tggcgatatt gatatcatgt ccttgaaacg 300
aatgctggag aaacttgag tccccaagac tcacctagag ctaaagaaat taattggaga 360
ggtgtccagt ggetccgggg agacgttcag ctaccctgac tttctcagga tgatgctggg 420
caagagatct gccatcctaa aaatgatcct gatgtatgag gaaaaagcga gagaaaggaa 480
aaccaacacg cccccagcc aagaaagccc tatctgagat gcctgatttg agggaaaagg 540

```

- 110 -

gatgatggga ttgaaggggt tctaataccc agatatggaa acagaagaca aaatcgtaag 600
 ccagagtcaa caaattaaat aaatttacc caaaaaaaaa 639

<210> 68

<211> 1799

<212> DNA

<213> Homo sapiens

<400> 68

gcttgaaccg gggaggtgga ggttgcagtg agctgagatc acgccattgt actccagcct 60
 gggcgacaga gcaagactcc atttcaaaaa aaaaaaaaaa aaaaaaaatc cactcatata 120
 aaaggtgagc tcagctcact ggtccatttc tcagtggctt ctccatcctc atttgcaaac 180
 ctgagaggga taaggcagtt gaacctgatg agcaagaatt ataacagcaa ggaaacatta 240
 atgcttagaa ttctgagatc cagcacaact cagtctgtgg gagctcagct cgctgcccag 300
 ggataggtat gacctatgtc tgccttaggc tgctgggaga tgccattctc cagtttcaga 360
 agcaggcagg gcaaaggtca agactgtggt attgggggtct tttggctctg aaggatcctg 420
 gaaccactga ttttggttta ttccctccag ggtctaaaga gaacaagagg tgctagctct 480
 taccaaaaca gatggtagag agagttgctg gctattttaa aagctctttc atcttttaat 540
 tcacctcttc ttttcacctc ttaaccact cctcaggaac agaacacttc taggactggg 600
 ggtcttttag ctccataagc aagtgagcag atgggacaag ttagtctttt ctccctagaa 660
 acaaagggga tgcccagtgg ttccctttg cttcccaacc taaaatttca agtttaataa 720
 aatagcaatt agcagaagtg accaaattgg gagataatta tcagtcatga ggaaagacac 780
 agatttcggt cataaagaat gtaagggcta taagtagaaa ctttctataa cctaaatgat 840
 gttatagaat tatttttgag caggagcaga aagattaaat atgatcactt catacttcta 900
 aatcagaaat aggaagatta aaaccacaga acagtttggtg atttctattg ctggtagcta 960
 ggtatcttac tctgtccact cttgttcaag tatctaactc ttctggaaac caaataggct 1020
 ttagaagaga ttatcctata ttctatcag tataatacta aaatgtaact ttttaatcat 1080
 ctggttttta aaagataaac agtttagccc atctctccag agagcaaaca taggaatatg 1140
 actcaggagc ctcctagggc ttatcatcag ccctcacacc cgcttcccc tccaaccac 1200
 agcctttgct tccaggtggc aggattacta ctttgctctc tcagcagcat ctactctagg 1260

- 111 -

catattgatc atttttagaca ctggggagaag agaacctcaa actaggagga aaagacagag 1320
cctccactta gttttgggag gggatggcag acagtcaagg agatgagcgt cctaaggcat 1380
gttgggatag ggtcagatgc accacccatg gagaggtttg tcaacacaaa gacatggaag 1440
gttagagggtt tgtcaacaaa aagacatgga aggttaggtt tgtcaacaca aagacatgga 1500
agattagagg tttgtcaaca caaagataca ggaagaatgg gctgcagaag atttagatgt 1560
tttccatttg ggcacatttt acttagctgg agaactaggt ttaaaacagc ctgggtagga 1620
aaattagaag caagctggat gcagtggctc atgcctgtaa tccaacact tttgggaggt 1680
ccaggcagga ggatcacttg ggcccaggag gtcaagcctg cagcgagctg agatcacacc 1740
actgcactcc agcctggggt gatagaacaa gaccctgtct caaaaaaaaaa aaaaaaaaaa 1799

<210> 69

<211> 660

<212> DNA

<213> Homo sapiens

<400> 69

atgcacgtga acggcaaagt ggcgctggtg accggcgcgg ctcagggcat aggcagagcc 60
tttgcagagg cgctgctgct taagggcgcc aaggtagcgc tgggtggattg gaatcttgaa 120
gcagggtgtac agtgtaaage tgccctggat gagcagtttg aacctcagaa gactctgttc 180
atccagtgcg atgtggctga ccagcaacaa ctgagagaca cttttagaaa agttgtagac 240
cactttggaa gactggacat tttggtcaat aatgctggag tgaataataa gaaaaactgg 300
gaaaaaactc tgcaaattaa tttggtttct gttatcagtg gaacctatct tggtttggtat 360
tacatgagta agcaaaatgg aggtgaaggc ggcatcatta tcaatatgtc atcttttagca 420
ggactcatgc ccgttgacaca gcagccggtt tattgtgctt caaagcatgg catagttgga 480
ttcacacgct cagcagcgcc caccattgat tgccaatgga ttgataacac tcattgaaga 540
tgatgcttta aatggtgcta ttatgaagat cacaacttct aaggggaattc attttcaaga 600
ctatgatata actccatttc aagcaaaaac ccaatgaaca gcttatgtgt tagccatagc 660

- 112 -

<210> 70

<211> 3257

<212> DNA

<213> Homo sapiens

<400> 70

aacaggcgtg acgccagttc taaacttgaa acaaaacaaa acttcaaagt acacccaaaat	60
agaacctcct taaagcataa atctcacgga gggctctcggc cgccagtgga aggagccacc	120
gcccccgccc cgacccatggc cgaggagctg gtcttagaga ggtgtgatct ggagctggag	180
accaatggcc gagaccacca cacggccgac ctgtgccggg agaagctggt ggtgcgacgg	240
ggccagccct tctggctgac cctgcacttt gagggccgca actaccaggc cagtgtagac	300
agtctcacct tcagtgtcgt gaccggccca gccctagcc aggaggccgg gaccaaggcc	360
cgttttccac taagagatgc tgtggaggag ggtgactgga cagccaccgt ggtggaccag	420
caagactgca ccctctcgtc gcagctcacc accccggcca acgcccccat cggcctgtat	480
cgctcagcc tggaggcctc cactggctac cagggatoca gctttgtgct gggccacttc	540
atthttgctct tcaacgcctg gtgcccagcg gatgctgtgt acctggactc ggaagaggag	600
cggcaggagt atgtcctcac ccagcagggc tttatctacc agggctcggc caagttcatc	660
aagaacatac cttggaattt tgggcagttt caagatggga tcctagacat ctgcctgatc	720
cttctagatg tcaaccccaa gttcctgaag aacgccggcc gtgactgctc ccggcgacgc	780
agccccgtct acgtgggccc ggtgggtagt ggcattggtca actgcaacga tgaccagggt	840
gtgctgctgg gacgctggga caacaactac ggggacggcg tcagccccat gtcttgatc	900
ggcagcgtgg acatcctgcg gcgctggaag aaccacggct gccagcgcgt caagtatggc	960
cagtgtctggg tcttcgcccgc cgtggcctgc acagtgtga ggtgcctagg catccctacc	1020
cgcgtcgtga ccaactacaa ctccggccat gaccagaaca gcaaccttct catcgagtac	1080
ttccgcaatg agtttgggga gatccagggt gacaagagcg agatgatctg gaacttccac	1140
tgctgggtgg agtcgtggat gaccaggccg gacctgcagc cggggtagca gggctggcag	1200
gccctggacc caacgccccca ggagaagagc gaaggaacgt actgctgtgg ccagttcca	1260
gttcgtgcca tcaaggaggg cgacctgagc accaagtacg atgcgccctt tgtctttgcg	1320
gaggtcaatg ccgacgtggt agactggatc cagcaggacg atgggtctgt gcacaaatcc	1380
atcaaccgtt ccctgatcgt tgggctgaag atcagcacta agagcgtggg ccgagacgag	1440

- 113 -

cgggaggata tcacccacac ctacaaatac ccagaggggt cctcagagga gagggaggcc 1500
ttcacaaggg cgaaccacct gaacaaactg gccgagaagg aggagacagg gatggccatg 1560
cggatccgtg tgggccagag catgaacatg ggcagtgact ttgacgtctt tgcccacatc 1620
accaacaaca ccgctgagga gtacgtctgc cgcctcctgc tctgtgcccg caccgtcagc 1680
tacaatggga tcttggggcc cgagtgtggc accaagtacc tgctcaacct aaccctggag 1740
cctttctctg agaagagcgt tcctctttgc atcctctatg agaaataccg tgactgcctt 1800
acggagtcca acctcatcaa ggtgcgggccc ctctcgtgg agccagttat caacagctac 1860
ctgctggctg agagggacct ctacctggag aatccagaaa tcaagatccg gatccttggg 1920
gagcccaagc agaaacgcaa gctggtggct gaggtgtccc tgcagaaccc gctcctgtg 1980
gccctggaag gctgcacctt cactgtggag ggggccggcc tgactgagga gcagaagacg 2040
gtggagatcc cagaccccgt ggaggcaggg gaggaagtta aggtgagaat ggacctcgtg 2100
ccgctccaca tgggcctcca caagctggtg gtgaacttcg agagcgacaa gctgaaggct 2160
gtgaagggtt tccggaatgt catcattggc cccgcctaag ggacccctgc tcccagcctg 2220
ctgagagccc ccacctgat cccaatcctt atccaagct agtgagcaaa atatgccctt 2280
tattgggccc cagaccccag ggcaggggtg gcagcctatg ggggctctcg gaaatggaat 2340
gtgcccctgg cccatctcag cctcctgagc ctgtgggtcc ccactcacc cctttgctgt 2400
gaggaatgct ctgtgccaga aacagtggga gccctgacct gtgctgactg gggctggggt 2460
gagagaggaa agacctacat tccctctect gccagatgc cctttggaaa gccattgacc 2520
accaccata ttgtttgate tacttcatag ctcttggag caggcaaaaa agggacagca 2580
tgcccttggc tggatcagga atccagctcc ctagactgca tcccgtacct ctccccatga 2640
ctgcaccag ctccaggggc ccttgggaca ccagagctg ggtggggaca gtgataggcc 2700
caaggtoccc tccacatccc agcagcccaa gcttaatagc cctcccctc aacctacca 2760
ttgtgaagca cctactatgt gctgggtgcc tcccacactt gctggggctc acggggcctc 2820
caaccattt aatcaccatg ggaaactgtt gtgggcgctg cttccaggat aaggagactg 2880
aggettagag agaggaggca gcccctcca caccagtggc ctctgtggtta taagcaaggc 2940
tgggtaatgt gaaggcccaa gagcagagtc tgggcctctg actctgagtc cactgctcca 3000
tttataacce cagcctgacc tgagactgtc gcagaggctg tctggggcct ttatcaaaaa 3060
aagactcagc caagacaagg aggtagagag gggactgggg gactgggagt cagagccctg 3120
gctgggttca ggtcccacgt ctggccagcg actgccttct cctctctggg cctttgtttc 3180
cttggttggtc agaggagtga ttgaacctgc tcctctccaa ggatcctctc cactccatgt 3240

- 114 -

ttgcaataca caattcc

3257

<210> 71

<211> 980

<212> DNA

<213> Homo sapiens

<400> 71

gctttcttgg gaagatggcg gctgtgtcgg tgtatgctcc accagttgga ggcttctctt	60
ttgataactg ccgcaggaat gccgtcttgg aagccgattt tgcaaagagg ggatacaagc	120
ttccaaaggt ccggaaaact ggcacgacca tcgctgggggt ggtctataag gatggcatag	180
ttcttggagc agatacaaga gcaactgaag ggatgggtgt tgctgacaag aactgttcaa	240
aaatacactt catatctcct aatatttatt gttgtggtgc tgggacagct gcagacacag	300
acatgacaac ccagctcatt tcttccaacc tggagctcca ctccctctcc actggccgtc	360
ttcccagagt tgtgacagcc aatcggatgc tgaagcagat gcttttcagg tatcaagggt	420
acattggtgc agccctagtt ttagggggag tagatgttac tggacctcac ctctacagca	480
tctatcctca tggatcaact gataagttgc cttatgtcac catgggttct ggctccttgg	540
cagcaatggc tgtatttgaa gataagttta ggccagacat ggaggaggag gaagccaaga	600
atctggtgag cgaagccatc gcagctggca tcttcaacga cctgggctcc ggaagcaaca	660
ttgacctctg cgtcatcagc aagaacaage tggattttct ccgcccatac acagtgccca	720
acaagaaggg gaccaggctt ggccggtaca ggtgtgagaa agggactact gcagtccctca	780
ctgagaaaaat cactcctctg gagattgagg tgctggaaga aacagtccaa acaatggaca	840
cttcctgaat ggcacagtg ggtggctggc cgcggttctg gaaggtggtg agcattgagg	900
cccagtaaga cactcatgtg gctagtgttt gccgaatgaa actcaactca ataaaaaaca	960
aaaaccaa at tgggcagctg	980

- 115 -

<210> 72

<211> 3992

<212> DNA

<213> Homo sapiens

<400> 72

```

ggcttcagga agggcagaca gagtgtccaa aagcgtgaga gcacgaagtg aggagaaggt      60
ggagaagaga gaagaggaag aggaagagga agagaggaag cggaggggaac tgcggccagg      120
ctaaaagggg aagaagagga tcagcccaag gaggaggaag aggaaaacaa gacaaacagc      180
cagtgcagag gagaggaacg tgtgtccagt gtcccgatcc ctgcggagct agtagctgag      240
agctctgtgc cctgggcacc ttgcagccct gcacctgcct gccacttccc caccgaggcc      300
atgggcccag gagttctgct gtcctgctg gtggccacag cttggcatgg tcagggaatc      360
ccagtgatag agcccagtgt ccccgagctg gtcgtgaagc caggagcaac ggtgaccttg      420
cgatgtgtgg gcaatggcag cgtggaatgg gatggccccg catcacctca ctggacctg      480
tactctgatg gctccagcag catcctcagc accaacaacg ctacctcca aaacacgggg      540
acctatcgct gcactgagcc tggagacccc ctgggaggca gcgccgccat ccacctctat      600
gtcaaagacc ctgcccggcc ctggaactg ctagcacagg aggtggtcgt gttegaggac      660
caggacgcac tactgccctg tctgctcaca gacccggtgc tggaagcagg cgtctcgctg      720
gtgctgtgct gtggccggcc cctcatgcgc cacaccaact actccttctc gccctggcat      780
ggcttcacca tocacagggc caagttcatt cagagccagg actatcaatg cagtgccttg      840
atgggtggca ggaaggtgat gtccatcagc atccggtga aagtgcagaa agtcatcca      900
gggccccccag ccttgacact ggtgcctgca gagctggtgc ggattcgagg ggaggctgcc      960
cagatcgtgt gctcagccag cagcgttgat gttaactttg atgtcttcct ccaacacaac     1020
aacactaagc togcaatccc tcaacaatct gactttcata ataaccgtta ccaaaaagtc     1080
ctgacctca acctcgatca agtagatttc caacatgccg gcaactactc ctgctgggcc     1140
agcaacgtgc agggcaagca ctccacctcc atgttcttcc gggtggtaga gagtgcctac     1200
ttgaacttga gctctgagca gaacctcatc caggaggtga ccgtggggga ggggctcaac     1260
ctcaaagtca tgggtggagge ctaccagggc ctgcaagggt ttaactggac ctacctggga     1320
cccttttctg accaccagcc tgagcccaag cttgctaatt ctaccaccaa ggacacatac     1380
aggcacacct tcacctctc tctgccccgc ctgaagccct ctgaggctgg ccgctactcc     1440

```

- 116 -

ttcctggcca gaaacccagg aggctggaga gctctgacgt ttgagctcac ccttcgatac	1500
ccccagagg taagcgatcat atggacattc atcaacggct ctggcaccct tttgtgtgct	1560
gcctctgggt acccccagcc caacgtgaca tggctgcagt gcagtggcca cactgatagg	1620
tgtgatgagg cccaagtgtc gcaggctctg gatgacccat accctgaggt cctgagccag	1680
gagcccttcc acaagggtgac ggtgcagagc ctgctgactg ttgagacctt agagcacaac	1740
caaacctacg agtgcagggc ccacaacagc gtggggagtg gctcctgggc cttcataccc	1800
atctctgcag gageccacac gcateccccg gatgagttcc tcttcacacc agtggtggtc	1860
gcctgcatgt ccatcatggc cttgctgctg ctgctgctcc tgctgctatt gtacaagtat	1920
aagcagaagc ccaagtacca ggtccgctgg aagatcatcg agagctatga gggcaacagt	1980
tatactttca tcgaccccac gcagctgcct tacaacgaga agtgggagtt cccccggaac	2040
aacctgcagt ttggtaagac cctcggagct ggagccttg ggaagggtgg ggaggccacg	2100
gcctttggtc tgggcaagga ggatgctgtc ctgaagggtg ctgtgaagat gctgaagtcc	2160
acggcccatg ctgatgagaa ggaggccctc atgtccgagc tgaagatcat gagccacctg	2220
ggccagcacg agaacatcgt caaccttctg ggagcctgta cccatggagg ccctgtactg	2280
gtcatcacgg agtactgttg ctatggcgac ctgctcaact ttctgcgaag gaaggctgag	2340
gccatgctgg gaccagcct gagccccggc caggaccccg agggaggcgt cgactataag	2400
aacatccacc tcgagaagaa atatgtccgc agggacagtg gcttctccag ccagggtgtg	2460
gacacctatg tggagatgag gcctgtctcc acttcttcaa atgactcctt ctctgagcaa	2520
gacctggaca aggaggatgg acggccctg gagctccggg acctgcttca cttctccagc	2580
caagtagccc agggcatggc cttcctcgtc tccaagaatt gcatccaccg ggacgtggca	2640
gcgcgtaacg tgctgttgac caatggatcat gtggccaaga ttggggactt cgggctggct	2700
agggacatca tgaatgactc caactacatt gtcaagggca atgcccgcct gcctgtgaag	2760
tggatggccc cagagagcat ctttgactgt gtctacacgg ttcagagcga cgtctggtcc	2820
tatggcatec tcctctggga gatcttctca cttgggctga atccctaccc tggcatcctg	2880
gtgaacagca agttctataa actggtgaag gatggatacc aaatggccca gcctgcattt	2940
gccccaaaga atatatacag catcatgcag gcctgctggg ccttggagcc caccacaga	3000
cccaccttcc agcagatctg ctcttctctt caggagcagg cccaagagga caggagagag	3060
cgggactata ccaatctgcc gagcagcagc agaagcgggtg gcagcggcag cagcagcagt	3120
gagctggagg aggagagctc tagtgagcac ctgacctgct gcgagcaagg ggatatcgcc	3180
cagcccttgc tgcagcccaa caactatcag ttctgctgag gagttgacga cagggagtac	3240

- 117 -

cactctcccc tcctccaaac ttcaactcct ccatggatgg ggcgacacgg ggagaacata 3300
 caaactctgc ctteggtcat ttactcaac agctcggccc agctctgaaa cttgggaagg 3360
 tgagggattc aggggaggtc agaggatccc acttctgag catgggceat cactgccagt 3420
 caggggctgg gggctgagcc ctcaccccc gcctccccta ctgttctcat ggtgttgcc 3480
 tcgtgtttgc tatgccaact agtagaacct tctttcctaa tccccttate ttcattgaaa 3540
 tggactgact ttatgcctat gaagtcccca ggagctacac tgatactgag aaaaccaggc 3600
 tctttggggc tagacagact ggcagagagt gagatctccc tctctgagag gagcagcaga 3660
 tgctcacaga ccacactcag ctcaggcccc ttggagcagg atggctcctc taagaatctc 3720
 acaggacctc ttagtctctg ccctatacgc cgccttact ccacagctc acccctccca 3780
 ccccatact ggtactgctg taatgagcca agtggcagct aaaagttggg ggtgttctgc 3840
 ccagtccegt cattctgggc tagaaggcag gggaccttgg cattggctgg ccacaccaag 3900
 caggaagcac aaactcccc aagctgactc atcctaacta acagtcacgc cgtgggatgt 3960
 ctctgtccac attaaactaa cagcattaat gc 3992

<210> 73

<211> 1490

<212> DNA

<213> Homo sapiens

<400> 73

ggggcagcgc agggcagacg gcggcaggag aagcaagatg aatgcaggct cagatcctgt 60
 ggtcatcgte tcggcggcgc ggaccatcat aggttccttc aatgggtgct tagctgctgt 120
 tcctgtccag gacctgggct ccactgtcat caaagaagtc ttgaagaggg ccactgtggc 180
 tocggaagat gtgtctgagg tcatctttgg acatgtcttg gcagcaggct gtgggcagaa 240
 tcctgttaga caagccagtg tgggtgcagg aattccctac tctgttccag catggagctg 300
 ccagatgate tgtgggtcag gcctaaaagc tgtgtgcctt gcagtccagt caatagggat 360
 aggagactcc agcattgtgg ttgcaggagg catggaaaat atgagcaagg ctcctcactt 420
 ggcttacttg agaacaggag taaagatagg tgagatgcca ctgactgaca gtatactctg 480
 tgatggtctt acagatgcat ttcacaactg tcatatgggt attacagctg aaaatgtagc 540
 cacaaaatgg caagtgagta gagaagatca ggacaagggt gcagttctgt ccagaaacag 600

- 118 -

gacagagaat gcacagaaag ctggccattt tgacaaagag attgtaccag ttttgggtgc 660
 aactagaaaa ggtcttattg aagttaaaac agatgagttt cctcgccatg ggagcaacat 720
 agaagccatg tccaagctaa agccttactt tcttactgat ggaacgggaa cagtcacccc 780
 agccaatgct tcaggaataa atgatgggtgc tgcagctggt gctcttatga agaagtcaga 840
 agctgataaa cgtgggctta cacctttagc acggatagtt tcctgggtccc aagtgggtgt 900
 ggagccttcc attatgggaa taggaccaat tccagccata aagcaagctg ttacaaaagc 960
 aggttgggtca ctggaagatg ttgacatatt tgaaatcaat gaagcctttg cagctgtctc 1020
 tgctgcaata gttaaagaac ttggattaaa ccagagagaag gtcaatattg aaggaggggc 1080
 tatagccttg ggccaccctc ttggagcatc tggctgtcga attcttgtga ccctgttaca 1140
 cacactggag agaatgggca gaagtcgtgg tgttgagcc ctgtgcattg ggggtgggat 1200
 gggaatagca atgtgtgttc agagagaatg acaatgtgtg ttcagagaga atgaattgct 1260
 taaactttga acaacctcaa tttcttttta aactaataaa gtactagggt gcaatatgtg 1320
 aaatcagagg accaaagtac agatggaaac catttcctac atcacaaaaa cccaagttta 1380
 cagcttgtagc tttactttaa tgtgtaatac tcaactcacg gtacaagaca attgcattta 1440
 acattgttat aaataaaaag aacatcagat caatcattaa aaaaaaaaaa 1490

<210> 74

<211> 1339

<212> DNA

<213> Homo sapiens

<400> 74

ttgcactcta gaagggacaa tggacttctg gctttggcca ctttacttcc tgccagtatc 60
 gggggccctg aggatcctcc cagaagtaaa ggtagagggg gagctgggag gatcagttac 120
 catcaagtgc ccacttctg aaatgcatgt gaggatatat ctgtgccggg agatggctgg 180
 atctggaaca tgtggtaccg tggatatccac caccaacttc atcaaggcag aatacaaggg 240
 ccgagttact ctgaagcaat acccacgcaa gaatctgttc ctagtggagg taacacagct 300
 gacagaaagt gacagcggag tctatgcctg cggagcgggc atgaacacag accggggaaa 360
 gaccagaaa gtcaccctga atgtccacag tgaatacgag ccatcatggg aagagcagcc 420
 aatgcctgag actccaaaat gggttcatct gccctatttg ttccagatgc ctgcatatgc 480
 cagttcttcc aaattcgtaa ccagagttac cacaccagct caaaggggca aggtccctcc 540

- 119 -

```

agttcaccac tcttccccca ccacccaaat caccaccgc cctcgagtgt ccagagcatc 600
ttcagtagca ggtgacaagc ccogaacctt cctgccatcc actacagcct caaaaatctc 660
agctctggag gggctgctca agccccagac gccagctac aaccaccaca ccaggctgca 720
caggcagaga gcactggact atggctcaca gtctgggagg gaaggccaag gatttcacat 780
cctgatcccg accatcctgg gccttttctt gctggaactt ctggggctgg tggtgaaaag 840
ggccgttgaa aggaggaaag ccctctccag gcggggccgc cgactggccg tgaggatgcg 900
cgccctggag agtcccaga ggccccgcgg gtcgccgcga ccgcgctccc aaaacaacat 960
ctacagcgcc tgcccggggc gcgctcgtgg agcggacgct gcaggcacag gggaagcccc 1020
cgttcccggc ccgggagcgc cgttgcccc cggcccgtg caggtgtctg aatctccctg 1080
gtcccatgcc ccatctctga agaccagctg tgaatacgtg agcctctacc accagcctgc 1140
cgccatgatg gaggacagtg attcagatga ctacatcaat gttcctgcct gacaactccc 1200
cagctatccc ccaaccccag gctcggactg tggtgccaag gagtctcatc tatctgctga 1260
tgtccaatac ctgcttcatg tgttctcaga gccctcatca ttcccatgcc ccatctcgat 1320
cccatcccca tctatctgt 1339

```

<210> 75

<211> 152

<212> PRT

<213> Homo sapiens

<400> 75

```

Met Ala Asn Leu Glu Arg Thr Phe Ile Ala Ile Lys Pro Asp Gly Val
1           5           10           15

```

```

Gln Arg Gly Leu Val Gly Glu Ile Ile Lys Arg Phe Glu Gln Lys Gly
20           25           30

```

```

Phe Arg Leu Val Ala Met Lys Phe Leu Arg Ala Ser Glu Glu His Leu
35           40           45

```

```

Lys Gln His Tyr Ile Asp Leu Lys Asp Arg Pro Phe Phe Pro Gly Leu
50           55           60

```

```

Val Lys Tyr Met Asn Ser Gly Pro Val Val Ala Met Val Trp Glu Gly

```


- 120 -

65		70		75		80
Leu Asn Val Val Lys Thr Gly Arg Val Met Leu Gly Glu Thr Asn Pro						
		85		90		95
Ala Asp Ser Lys Pro Gly Thr Ile Arg Gly Asp Phe Cys Ile Gln Val						
		100		105		110
Gly Arg Asn Ile Ile His Gly Ser Asp Ser Val Lys Ser Ala Glu Lys						
		115		120		125
Glu Ile Ser Leu Trp Phe Lys Pro Glu Glu Leu Val Asp Tyr Lys Ser						
		130		135		140
Cys Ala His Asp Trp Val Tyr Glu						
145		150				

<210> 76

<211> 538

<212> PRT

<213> Homo sapiens

<400> 76

Gly Asn Ser Ile Ser Leu Asp Phe Glu Pro Ser Ile Glu Tyr Gln Phe																
1				5				10						15		
Val Glu Arg Leu Glu Glu Arg Tyr Lys Cys Ala Phe Cys His Ser Val																
			20					25						30		
Leu His Asn Pro His Gln Thr Gly Cys Gly His Arg Phe Cys Gln His																
		35					40					45				
Cys Ile Leu Ser Leu Arg Glu Leu Asn Thr Val Pro Ile Cys Pro Val																
		50				55				60						
Asp Lys Glu Val Ile Lys Ser Gln Glu Val Phe Lys Asp Asn Cys Cys																
65					70			75						80		
Lys Arg Glu Val Leu Asn Leu Tyr Val Tyr Cys Ser Asn Ala Pro Gly																
				85			90							95		

- 121 -

Cys Asn Ala Lys Val Ile Leu Gly Arg Tyr Gln Asp His Leu Gln Gln
100 105 110

Cys Leu Phe Gln Pro Val Gln Cys Ser Asn Glu Lys Cys Arg Glu Pro
115 120 125

Val Leu Arg Lys Asp Leu Lys Glu His Leu Ser Ala Ser Cys Gln Phe
130 135 140

Arg Lys Glu Lys Cys Leu Tyr Cys Lys Lys Asp Val Val Val Ile Asn
145 150 155 160

Leu Gln Asn His Glu Glu Asn Leu Cys Pro Glu Tyr Pro Val Phe Cys
165 170 175

Pro Asn Asn Cys Ala Lys Ile Ile Leu Lys Thr Glu Val Asp Glu His
180 185 190

Leu Ala Val Cys Pro Glu Ala Glu Gln Asp Cys Pro Phe Lys His Tyr
195 200 205

Gly Cys Ala Val Thr Asp Lys Arg Arg Asn Leu Gln Gln His Glu His
210 215 220

Ser Ala Leu Arg Glu His Met Arg Leu Val Leu Glu Lys Asn Val Gln
225 230 235 240

Leu Glu Glu Gln Ile Ser Asp Leu His Lys Ser Leu Glu Gln Lys Glu
245 250 255

Ser Lys Ile Gln Gln Leu Ala Glu Thr Ile Lys Lys Leu Glu Lys Glu
260 265 270

Phe Lys Gln Phe Ala Gln Leu Phe Gly Lys Asn Gly Ser Phe Leu Pro
275 280 285

Asn Ile Gln Val Phe Ala Ser His Ile Asp Lys Ser Ala Trp Leu Glu
290 295 300

Ala Gln Val His Gln Leu Leu Gln Met Val Asn Gln Gln Gln Asn Lys
305 310 315 320

Phe Asp Leu Arg Pro Leu Met Glu Ala Val Asp Thr Val Lys Gln Lys
325 330 335

- 122 -

Ile Thr Leu Leu Glu Asn Asn Asp Gln Arg Leu Ala Val Leu Glu Glu
340 345 350

Glu Thr Asn Lys His Asp Thr His Ile Asn Ile His Lys Ala Gln Leu
355 360 365

Ser Lys Asn Glu Glu Arg Phe Lys Leu Leu Glu Gly Thr Cys Tyr Asn
370 375 380

Gly Lys Leu Ile Trp Lys Val Thr Asp Tyr Lys Met Lys Lys Arg Glu
385 390 395 400

Ala Val Asp Gly His Thr Val Ser Ile Phe Ser Gln Ser Phe Tyr Thr
405 410 415

Ser Arg Cys Gly Tyr Arg Leu Cys Ala Arg Ala Tyr Leu Asn Gly Asp
420 425 430

Gly Ser Gly Arg Gly Ser His Leu Ser Leu Tyr Phe Val Val Met Arg
435 440 445

Gly Glu Phe Asp Ser Leu Leu Gln Trp Pro Phe Arg Gln Arg Val Thr
450 455 460

Leu Met Leu Leu Asp Gln Ser Gly Lys Lys Asn Ile Met Glu Thr Phe
465 470 475 480

Lys Pro Asp Pro Asn Ser Ser Ser Phe Lys Arg Pro Asp Gly Glu Met
485 490 495

Asn Ile Ala Ser Gly Cys Pro Arg Phe Val Ala His Ser Val Leu Glu
500 505 510

Asn Ala Lys Asn Ala Tyr Ile Lys Asp Asp Thr Leu Phe Leu Lys Val
515 520 525

Ala Val Asp Leu Thr Asp Leu Glu Asp Leu
530 535

<210> 77

<211> 583

<212> PRT

- 123 -

<213> Homo sapiens

<400> 77

Met Pro Lys Pro Ile Asn Val Arg Val Thr Thr Met Asp Ala Glu Leu
1 5 10 15

Glu Phe Ala Ile Gln Pro Asn Thr Thr Gly Lys Gln Leu Phe Asp Gln
20 25 30

Val Val Lys Thr Val Gly Leu Arg Glu Val Trp Phe Phe Gly Leu Gln
35 40 45

Tyr Val Asp Ser Lys Gly Tyr Ser Thr Trp Leu Lys Leu Asn Lys Lys
50 55 60

Val Thr Gln Gln Asp Val Lys Lys Glu Asn Pro Leu Gln Phe Lys Phe
65 70 75 80

Arg Ala Lys Phe Phe Pro Glu Asp Val Ser Glu Glu Leu Ile Gln Glu
85 90 95

Ile Thr Gln Arg Leu Phe Phe Leu Gln Val Lys Glu Ala Ile Leu Asn
100 105 110

Asp Glu Ile Tyr Cys Pro Pro Glu Thr Ala Val Leu Leu Ala Ser Tyr
115 120 125

Ala Val Gln Ala Lys Tyr Gly Asp Tyr Asn Lys Glu Ile His Lys Pro
130 135 140

Gly Tyr Leu Ala Asn Asp Arg Leu Leu Pro Gln Arg Val Leu Glu Gln
145 150 155 160

His Lys Leu Thr Lys Glu Gln Trp Glu Glu Arg Ile Gln Asn Trp His
165 170 175

Glu Glu His Arg Gly Met Leu Arg Glu Asp Ser Met Met Glu Tyr Leu
180 185 190

Lys Ile Ala Gln Asp Leu Glu Met Tyr Gly Val Asn Tyr Phe Glu Ile
195 200 205

Lys Asn Lys Lys Gly Thr Glu Leu Trp Leu Gly Val Asp Ala Leu Gly

- 124 -

210	215	220
Leu Asn Ile Tyr Glu His Asp Asp Lys Leu Thr Pro Lys Ile Gly Phe 225 230 235 240		
Pro Trp Ser Glu Ile Arg Asn Ile Ser Phe Asn Asp Lys Lys Phe Val 245 250 255		
Ile Lys Pro Ile Asp Lys Lys Ala Pro Asp Phe Val Phe Tyr Ala Pro 260 265 270		
Arg Leu Arg Ile Asn Lys Arg Ile Leu Ala Leu Cys Met Gly Asn His 275 280 285		
Glu Leu Tyr Met Arg Arg Arg Lys Pro Asp Thr Ile Glu Val Gln Gln 290 295 300		
Met Lys Ala Gln Ala Arg Glu Glu Lys His Gln Lys Gln Leu Glu Arg 305 310 315 320		
Ala Gln Leu Glu Asn Glu Lys Lys Lys Arg Glu Ile Ala Glu Lys Glu 325 330 335		
Lys Glu Arg Ile Glu Arg Glu Lys Glu Glu Leu Met Glu Arg Leu Lys 340 345 350		
Gln Ile Glu Glu Gln Thr Ile Lys Ala Gln Lys Glu Leu Glu Glu Gln 355 360 365		
Thr Arg Lys Ala Leu Glu Leu Asp Gln Glu Arg Lys Arg Ala Lys Glu 370 375 380		
Glu Ala Glu Arg Leu Glu Lys Glu Arg Arg Ala Ala Glu Glu Ala Lys 385 390 395 400		
Ser Ala Ile Ala Lys Gln Ala Ala Asp Gln Met Lys Asn Gln Glu Gln 405 410 415		
Leu Ala Ala Glu Leu Ala Glu Phe Thr Ala Lys Ile Ala Leu Leu Glu 420 425 430		
Glu Ala Lys Lys Lys Lys Glu Glu Glu Ala Thr Glu Trp Gln His Lys 435 440 445		

- 125 -

Ala Phe Ala Ala Gln Glu Asp Leu Glu Lys Thr Lys Glu Glu Leu Lys
 450 455 460

Thr Val Met Ser Ala Pro Pro Pro Pro Pro Pro Pro Val Ile Pro
 465 470 475 480

Pro Thr Glu Asn Glu His Asp Glu His Asp Glu Asn Asn Ala Glu Ala
 485 490 495

Ser Ala Glu Leu Ser Asn Glu Gly Val Met Asn His Arg Ser Glu Glu
 500 505 510

Glu Arg Val Thr Glu Thr Gln Lys Asn Glu Arg Val Lys Lys Gln Leu
 515 520 525

Gln Ala Leu Ser Ser Glu Leu Ala Gln Ala Arg Asp Glu Thr Lys Lys
 530 535 540

Thr Gln Asn Asp Val Leu His Ala Glu Asn Val Lys Ala Gly Arg Asp
 545 550 555 560

Lys Tyr Lys Thr Leu Arg Gln Ile Arg Gln Gly Asn Thr Lys Gln Arg
 565 570 575

Ile Asp Glu Phe Glu Ala Met
 580

<210> 78

<211> 580

<212> PRT

<213> Homo sapiens

<400> 78

Met Asn Phe Leu Arg Arg Arg Leu Ser Asp Ser Ser Phe Met Ala Asn
 1 5 10 15

Leu Pro Asn Gly Tyr Met Thr Asp Leu Gln Arg Pro Asp Ser Ser Thr
 20 25 30

Ser Ser Pro Ala Ser Pro Ala Met Glu Arg Arg His Pro Gln Pro Leu
 35 40 45

- 126 -

Ala Ala Ser Phe Ser Ser Pro Gly Ser Ser Leu Phe Ser Ser Leu Ser
50 55 60

Ser Ala Met Lys Gln Ala Pro Gln Ala Thr Ser Gly Leu Met Glu Pro
65 70 75 80

Pro Gly Pro Ser Thr Pro Ile Val Gln Arg Pro Arg Ile Leu Leu Val
85 90 95

Ile Asp Asp Ala His Thr Asp Trp Ser Lys Tyr Phe His Gly Lys Lys
100 105 110

Val Asn Gly Glu Ile Glu Ile Arg Val Glu Gln Ala Glu Phe Ser Glu
115 120 125

Leu Asn Leu Ala Ala Tyr Val Thr Gly Gly Cys Met Val Asp Met Gln
130 135 140

Val Val Arg Asn Gly Thr Lys Val Val Ser Arg Ser Phe Lys Pro Asp
145 150 155 160

Phe Ile Leu Val Arg Gln His Ala Tyr Ser Met Ala Leu Gly Glu Asp
165 170 175

Tyr Arg Ser Leu Val Ile Gly Leu Gln Tyr Gly Gly Leu Pro Ala Val
180 185 190

Asn Ser Leu Tyr Ser Val Tyr Asn Phe Cys Ser Lys Pro Trp Val Phe
195 200 205

Ser Gln Leu Ile Lys Ile Phe His Ser Leu Gly Pro Glu Lys Phe Pro
210 215 220

Leu Val Glu Gln Thr Phe Phe Pro Asn His Lys Pro Met Val Thr Ala
225 230 235 240

Pro His Phe Pro Val Val Val Lys Leu Gly His Ala His Ala Gly Met
245 250 255

Gly Lys Ile Lys Val Glu Asn Gln Leu Asp Phe Gln Asp Ile Thr Ser
260 265 270

Val Val Ala Met Ala Lys Thr Tyr Ala Thr Thr Glu Ala Phe Ile Asp
275 280 285

- 127 -

Ser Lys Tyr Asp Ile Arg Ile Gln Lys Ile Gly Ser Asn Tyr Lys Ala
 290 295 300

Tyr Met Arg Thr Ser Ile Ser Gly Asn Trp Lys Ala Asn Thr Gly Ser
 305 310 315 320

Ala Met Leu Glu Gln Val Ala Met Thr Glu Arg Tyr Arg Leu Trp Val
 325 330 335

Asp Ser Cys Ser Glu Met Phe Gly Gly Leu Asp Ile Cys Ala Val Lys
 340 345 350

Ala Val His Ser Lys Asp Gly Arg Asp Tyr Ile Ile Glu Val Met Asp
 355 360 365

Ser Ser Met Pro Leu Ile Gly Glu His Val Glu Glu Asp Arg Gln Leu
 370 375 380

Met Ala Asp Leu Val Val Ser Lys Met Ser Gln Leu Pro Met Pro Gly
 385 390 395 400

Gly Thr Ala Pro Ser Pro Leu Arg Pro Trp Ala Pro Gln Ile Lys Ser
 405 410 415

Ala Lys Ser Pro Gly Gln Ala Gln Leu Gly Pro Gln Leu Gly Gln Pro
 420 425 430

Gln Pro Arg Pro Pro Pro Gln Gly Gly Pro Arg Gln Ala Gln Ser Pro
 435 440 445

Gln Pro Gln Arg Ser Gly Ser Pro Ser Gln Gln Arg Leu Ser Pro Gln
 450 455 460

Gly Gln Gln Pro Leu Ser Pro Gln Ser Gly Ser Pro Gln Gln Gln Arg
 465 470 475 480

Ser Pro Gly Ser Pro Gln Leu Ser Arg Ala Ser Ser Gly Ser Ser Pro
 485 490 495

Asn Gln Ala Ser Lys Pro Gly Ala Thr Leu Ala Ser Gln Pro Arg Pro
 500 505 510

Pro Val Gln Gly Arg Ser Thr Ser Gln Gln Gly Glu Glu Ser Lys Lys

- 128 -

515 520 525
 Pro Ala Pro Pro His Pro His Leu Asn Lys Ser Gln Ser Leu Thr Asn
 530 535 540

 Ser Leu Ser Thr Ser Asp Thr Ser Gln Arg Gly Thr Pro Ser Glu Asp
 545 550 555 560

 Glu Ala Lys Ala Glu Thr Ile Arg Asn Leu Arg Lys Ser Phe Ala Ser
 565 570 575

 Leu Phe Ser Asp
 580

<210> 79

<211> 641

<212> PRT

<213> Homo sapiens

<400> 79

Met Ala Lys Ala Ala Ala Ile Gly Ile Asp Leu Gly Thr Thr Tyr Ser
 1 5 10 15

 Cys Val Gly Val Phe Gln His Gly Lys Val Glu Ile Ile Ala Asn Asp
 20 25 30

 Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr Glu
 35 40 45

 Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Leu Asn Pro Gln
 50 55 60

 Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe Gly Asp
 65 70 75 80

 Pro Val Val Gln Ser Asp Met Lys His Trp Pro Phe Gln Val Ile Asn
 85 90 95

 Asp Gly Asp Lys Pro Lys Val Gln Val Ser Tyr Lys Gly Glu Thr Lys
 100 105 110

- 129 -

Ala Phe Tyr Pro Glu Glu Ile Ser Ser Met Val Leu Thr Lys Met Lys
 115 120 125

Glu Ile Ala Glu Ala Tyr Leu Gly Tyr Pro Val Thr Asn Ala Val Ile
 130 135 140

Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr Lys Asp
 145 150 155 160

Ala Gly Val Ile Ala Gly Leu Asn Val Leu Arg Ile Ile Asn Glu Pro
 165 170 175

Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Arg Thr Gly Lys Gly Glu
 180 185 190

Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp Val Ser
 195 200 205

Ile Leu Thr Ile Asp Asp Gly Ile Phe Glu Val Lys Ala Thr Ala Gly
 210 215 220

Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val Asn His
 225 230 235 240

Phe Val Glu Glu Phe Lys Arg Lys His Lys Lys Asp Ile Ser Gln Asn
 245 250 255

Lys Arg Ala Val Arg Arg Leu Arg Thr Ala Cys Glu Arg Ala Lys Arg
 260 265 270

Thr Leu Ser Ser Ser Thr Gln Ala Ser Leu Glu Ile Asp Ser Leu Phe
 275 280 285

Glu Gly Ile Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe Glu Glu
 290 295 300

Leu Cys Ser Asp Leu Phe Arg Ser Thr Leu Glu Pro Val Glu Lys Ala
 305 310 315 320

Leu Arg Asp Ala Lys Leu Asp Lys Ala Gln Ile His Asp Leu Val Leu
 325 330 335

Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu Gln Asp
 340 345 350

- 130 -

Phe Phe Asn Gly Arg Asp Leu Asn Lys Ser Ile Asn Pro Asp Glu Ala
 355 360 365

Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu Met Gly Asp Lys
 370 375 380

Ser Glu Asn Val Gln Asp Leu Leu Leu Leu Asp Val Ala Pro Leu Ser
 385 390 395 400

Leu Gly Leu Glu Thr Ala Gly Gly Val Met Thr Ala Leu Ile Lys Arg
 405 410 415

Asn Ser Thr Ile Pro Thr Lys Gln Thr Gln Ile Phe Thr Thr Tyr Ser
 420 425 430

Asp Asn Gln Pro Gly Val Leu Ile Gln Val Tyr Glu Gly Glu Arg Ala
 435 440 445

Met Thr Lys Asp Asn Asn Leu Leu Gly Arg Phe Glu Leu Ser Gly Ile
 450 455 460

Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Ile
 465 470 475 480

Asp Ala Asn Gly Ile Leu Asn Val Thr Ala Thr Asp Lys Ser Thr Gly
 485 490 495

Lys Ala Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu Ser Lys
 500 505 510

Glu Glu Ile Glu Arg Met Val Gln Glu Ala Glu Lys Tyr Lys Ala Glu
 515 520 525

Asp Glu Val Gln Arg Glu Arg Val Ser Ala Lys Asn Ala Leu Glu Ser
 530 535 540

Tyr Ala Phe Asn Met Lys Ser Ala Val Glu Asp Glu Gly Leu Lys Gly
 545 550 555 560

Lys Ile Ser Glu Ala Asp Lys Lys Lys Val Leu Asp Lys Cys Gln Glu
 565 570 575

Val Ile Ser Trp Leu Asp Ala Asn Thr Leu Ala Glu Lys Asp Glu Phe
 580 585 590

- 131 -

Glu His Lys Arg Lys Glu Leu Glu Gln Val Cys Asn Pro Ile Ile Ser
 595 600 605

Gly Leu Tyr Gln Gly Ala Gly Gly Pro Gly Pro Gly Gly Phe Gly Ala
 610 615 620

Gln Gly Pro Lys Gly Gly Ser Gly Ser Gly Pro Thr Ile Glu Glu Val
 625 630 635 640

Asp

<210> 80

<211> 1940

<212> PRT

<213> Homo sapiens

<400> 80

Met Ser Ser Asp Thr Glu Met Glu Val Phe Gly Ile Ala Ala Pro Phe
 1 5 10 15

Leu Arg Lys Ser Glu Lys Glu Arg Ile Glu Ala Gln Asn Gln Pro Phe
 20 25 30

Asp Ala Lys Thr Tyr Cys Phe Val Val Asp Ser Lys Glu Glu Tyr Ala
 35 40 45

Lys Gly Lys Ile Lys Ser Ser Gln Asp Gly Lys Val Thr Val Glu Thr
 50 55 60

Glu Asp Asn Arg Thr Leu Val Val Lys Pro Glu Asp Val Tyr Ala Met
 65 70 75 80

Asn Pro Pro Lys Phe Asp Arg Ile Glu Asp Met Ala Met Leu Thr His
 85 90 95

Leu Asn Glu Pro Ala Val Leu Tyr Asn Leu Lys Asp Arg Tyr Thr Ser
 100 105 110

Trp Met Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Thr Val Asn Pro

- 132 -

115						120						125					
Tyr	Lys	Trp	Leu	Pro	Val	Tyr	Asn	Pro	Glu	Val	Val	Glu	Gly	Tyr	Arg		
130						135						140					
Gly	Lys	Lys	Arg	Gln	Glu	Ala	Pro	Pro	His	Ile	Phe	Ser	Ile	Ser	Asp		
145			150						155			160					
Asn	Ala	Tyr	Gln	Phe	Met	Leu	Thr	Asp	Arg	Glu	Asn	Gln	Ser	Ile	Leu		
			165						170			175					
Ile	Thr	Gly	Glu	Ser	Gly	Ala	Gly	Lys	Thr	Val	Asn	Thr	Lys	Arg	Val		
			180						185			190					
Ile	Gln	Tyr	Phe	Ala	Thr	Ile	Ala	Ala	Thr	Gly	Asp	Leu	Ala	Lys	Lys		
195						200						205					
Lys	Asp	Ser	Lys	Met	Lys	Gly	Thr	Leu	Glu	Asp	Gln	Ile	Ile	Ser	Ala		
210						215						220					
Asn	Pro	Leu	Leu	Glu	Ala	Phe	Gly	Asn	Ala	Lys	Thr	Val	Arg	Asn	Asp		
225			230						235			240					
Asn	Ser	Ser	Arg	Phe	Gly	Lys	Phe	Ile	Arg	Ile	His	Phe	Gly	Thr	Thr		
			245						250			255					
Gly	Lys	Leu	Ala	Ser	Ala	Asp	Ile	Glu	Thr	Tyr	Leu	Leu	Glu	Lys	Ser		
			260						265			270					
Arg	Val	Thr	Phe	Gln	Leu	Lys	Ala	Glu	Arg	Ser	Tyr	His	Ile	Phe	Tyr		
275						280						285					
Gln	Ile	Leu	Ser	Asn	Lys	Lys	Pro	Glu	Leu	Ile	Glu	Leu	Leu	Leu	Ile		
290						295						300					
Thr	Thr	Asn	Pro	Tyr	Asp	Tyr	Pro	Phe	Ile	Ser	Gln	Gly	Glu	Ile	Leu		
305			310						315			320					
Val	Ala	Ser	Ile	Asp	Asp	Arg	Glu	Glu	Leu	Leu	Ala	Thr	Asp	Ser	Ala		
			325						330			335					
Ile	Asp	Ile	Leu	Gly	Phe	Thr	Pro	Glu	Glu	Lys	Ser	Gly	Leu	Tyr	Lys		
			340						345			350					

- 133 -

Leu Thr Gly Ala Val Met His Tyr Gly Asn Met Lys Phe Lys Gln Lys
 355 360 365

Gln Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Val Ala Asp Lys
 370 375 380

Thr Ala Tyr Leu Met Gly Leu Asn Ser Ser Asp Leu Leu Lys Ala Leu
 385 390 395 400

Cys Phe Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly Gln
 405 410 415

Thr Val Asp Gln Val His His Ala Val Asn Ala Leu Ser Lys Ser Val
 420 425 430

Tyr Glu Lys Leu Phe Leu Trp Met Val Thr Arg Ile Asn Gln Gln Leu
 435 440 445

Asp Thr Lys Leu Pro Arg Gln His Phe Ile Gly Val Leu Asp Ile Ala
 450 455 460

Gly Phe Glu Ile Phe Glu Tyr Asn Ser Leu Glu Gln Leu Cys Ile Asn
 465 470 475 480

Phe Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe Val
 485 490 495

Leu Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile
 500 505 510

Asp Phe Gly Met Asp Leu Ala Ala Cys Ile Glu Leu Ile Glu Lys Pro
 515 520 525

Met Gly Ile Phe Ser Ile Leu Glu Glu Glu Cys Met Phe Pro Lys Ala
 530 535 540

Thr Asp Thr Ser Phe Lys Asn Lys Leu Tyr Asp Gln His Leu Gly Lys
 545 550 555 560

Ser Asn Asn Phe Gln Lys Pro Lys Val Val Lys Gly Arg Ala Glu Ala
 565 570 575

His Phe Ser Leu Ile His Tyr Ala Gly Thr Val Asp Tyr Ser Val Ser
 580 585 590

- 134 -

Gly Trp Leu Glu Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Gly
 595 600 605

Leu Tyr Gln Lys Ser Ser Asn Arg Leu Leu Ala His Leu Tyr Ala Thr
 610 615 620

Phe Ala Thr Ala Asp Ala Asp Ser Gly Lys Lys Lys Val Ala Lys Lys
 625 630 635 640

Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Leu Phe Arg Glu Asn Leu
 645 650 655

Asn Lys Leu Met Ser Asn Leu Arg Thr Thr His Pro His Phe Val Arg
 660 665 670

Cys Ile Ile Pro Asn Glu Thr Lys Thr Pro Gly Ala Met Glu His Ser
 675 680 685

Leu Val Leu His Gln Leu Arg Cys Asn Gly Val Leu Glu Gly Ile Arg
 690 695 700

Ile Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Lys
 705 710 715 720

Gln Arg Tyr Arg Val Leu Asn Ala Ser Ala Ile Leu Glu Gly Gln Phe
 725 730 735

Ile Asp Ser Lys Lys Ala Cys Glu Lys Leu Leu Ala Ser Ile Asp Ile
 740 745 750

Asp His Thr Gln Tyr Lys Phe Gly His Thr Lys Val Phe Phe Lys Ala
 755 760 765

Gly Leu Leu Gly Thr Leu Glu Glu Met Arg Asp Asp Arg Leu Ala Lys
 770 775 780

Leu Ile Thr Arg Thr Gln Ala Val Cys Arg Gly Phe Leu Met Arg Val
 785 790 795 800

Glu Phe Gln Lys Met Val Gln Arg Arg Glu Ser Ile Phe Cys Ile Gln
 805 810 815

Tyr Asn Ile Arg Ser Phe Met Asn Val Lys His Trp Pro Trp Met Lys
 820 825 830

- 135 -

Leu Phe Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Thr Glu Lys
835 840 845

Glu Met Ala Thr Met Lys Glu Glu Phe Gln Lys Thr Lys Asp Glu Leu
850 855 860

Ala Lys Ser Glu Ala Lys Arg Lys Glu Leu Glu Glu Lys Leu Val Thr
865 870 875 880

Leu Val Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Ser
885 890 895

Glu Asn Leu Leu Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Ala
900 905 910

Lys Phe Gln Leu Glu Ala Lys Ile Lys Glu Val Thr Glu Arg Ala Glu
915 920 925

Asp Glu Glu Glu Ile Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu
930 935 940

Glu Asp Glu Cys Ser Glu Leu Lys Lys Asp Ile Asp Asp Leu Glu Leu
945 950 955 960

Thr Leu Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val
965 970 975

Lys Asn Leu Thr Glu Glu Leu Ser Gly Leu Asp Glu Thr Ile Ala Lys
980 985 990

Leu Thr Arg Glu Lys Lys Ala Leu Gln Glu Ala His Gln Gln Ala Leu
995 1000 1005

Asp Asp Leu Gln Ala Glu Glu Asp Lys Val Asn Ser Leu Asn Lys
1010 1015 1020

Thr Lys Ser Lys Leu Glu Gln Gln Val Glu Asp Leu Glu Ser Ser
1025 1030 1035

Leu Glu Gln Glu Lys Lys Leu Arg Val Asp Leu Glu Arg Asn Lys
1040 1045 1050

- 136 -

Arg Lys Leu Glu Gly Asp Leu Lys Leu Ala Gln Glu Ser Ile Leu
1055 1060 1065

Asp Leu Glu Asn Asp Lys Gln Gln Leu Asp Glu Arg Leu Lys Lys
1070 1075 1080

Lys Asp Phe Glu Tyr Cys Gln Leu Gln Ser Lys Val Glu Asp Glu
1085 1090 1095

Gln Thr Leu Gly Leu Gln Phe Gln Lys Lys Ile Lys Glu Leu Gln
1100 1105 1110

Ala Arg Ile Glu Glu Leu Glu Glu Glu Ile Glu Ala Glu Arg Ala
1115 1120 1125

Thr Arg Ala Lys Thr Glu Lys Gln Arg Ser Asp Tyr Ala Arg Glu
1130 1135 1140

Leu Glu Glu Leu Ser Glu Arg Leu Glu Glu Ala Gly Gly Val Thr
1145 1150 1155

Ser Thr Gln Ile Glu Leu Asn Lys Lys Arg Glu Ala Glu Phe Leu
1160 1165 1170

Lys Leu Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala
1175 1180 1185

Met Val Ala Thr Leu Arg Lys Lys His Ala Asp Ser Val Ala Glu
1190 1195 1200

Leu Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys Gln Lys Leu
1205 1210 1215

Glu Lys Glu Lys Ser Glu Phe Lys Leu Glu Ile Asp Asp Leu Ser
1220 1225 1230

Ser Ser Met Glu Ser Val Ser Lys Ser Lys Ala Asn Leu Glu Lys
1235 1240 1245

Ile Cys Arg Thr Leu Glu Asp Gln Leu Ser Glu Ala Arg Gly Lys
1250 1255 1260

Asn Glu Glu Ile Gln Arg Ser Leu Ser Glu Leu Thr Thr Gln Lys
1265 1270 1275

- 137 -

Ser Arg Leu Gln Thr Glu Ala Gly Glu Leu Ser Arg Gln Leu Glu
1280 1285 1290

Glu Lys Glu Ser Ile Val Ser Gln Leu Ser Arg Ser Lys Gln Ala
1295 1300 1305

Phe Thr Gln Gln Thr Glu Glu Leu Lys Arg Gln Leu Glu Glu Glu
1310 1315 1320

Asn Lys Ala Lys Asn Ala Leu Ala His Ala Leu Gln Ser Ser Arg
1325 1330 1335

His Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu Glu Gln Glu
1340 1345 1350

Gly Lys Ala Glu Leu Gln Arg Ala Leu Ser Lys Ala Asn Ser Glu
1355 1360 1365

Val Ala Gln Trp Arg Thr Lys Tyr Glu Thr Asp Ala Ile Gln Arg
1370 1375 1380

Thr Glu Glu Leu Glu Glu Ala Gln Glu Lys Leu Ala Gln Arg Leu
1385 1390 1395

Gln Asp Ser Glu Glu Gln Val Glu Ala Val Asn Ala Lys Cys Ala
1400 1405 1410

'Ser Leu Glu Lys Thr Lys Gln Arg Leu Gln Gly Glu Val Glu Asp
1415 1420 1425

Leu Met Val Asp Val Glu Arg Ala Asn Ser Leu Ala Ala Ala Leu
1430 1435 1440

Asp Lys Lys Gln Arg Asn Phe Asp Lys Val Leu Ala Glu Trp Lys
1445 1450 1455

Thr Lys Cys Glu Glu Ser Gln Ala Glu Leu Glu Ala Ser Leu Lys
1460 1465 1470

Glu Ser Arg Ser Leu Ser Thr Glu Leu Phe Lys Leu Lys Asn Ala
1475 1480 1485

- 138 -

Tyr Glu Glu Ala Leu Asp Gln Leu Glu Thr Val Lys Arg Glu Asn
1490 1495 1500

Lys Asn Leu Glu Gln Glu Ile Ala Asp Leu Thr Glu Gln Ile Ala
1505 1510 1515

Glu Asn Gly Lys Thr Ile His Glu Leu Glu Lys Ser Arg Lys Gln
1520 1525 1530

Ile Glu Leu Glu Lys Ala Asp Ile Gln Leu Ala Leu Glu Glu Ala
1535 1540 1545

Glu Ala Ala Leu Glu His Glu Glu Ala Lys Ile Leu Arg Ile Gln
1550 1555 1560

Leu Glu Leu Thr Gln Val Lys Ser Glu Ile Asp Arg Lys Ile Ala
1565 1570 1575

Glu Lys Asp Glu Glu Ile Glu Gln Leu Lys Arg Asn Tyr Gln Arg
1580 1585 1590

Thr Val Glu Thr Met Gln Ser Ala Leu Asp Ala Glu Val Arg Ser
1595 1600 1605

Arg Asn Glu Ala Ile Arg Leu Lys Lys Lys Met Glu Gly Asp Leu
1610 1615 1620

Asn Glu Ile Glu Ile Gln Leu Ser His Ala Asn Arg Gln Ala Ala
1625 1630 1635

Glu Thr Leu Lys His Leu Arg Ser Val Gln Gly Gln Leu Lys Asp
1640 1645 1650

Thr Gln Leu His Leu Asp Asp Ala Leu Arg Gly Gln Glu Asp Leu
1655 1660 1665

Lys Glu Gln Leu Ala Ile Val Glu Arg Arg Ala Asn Leu Leu Gln
1670 1675 1680

Ala Glu Val Glu Glu Leu Arg Ala Thr Leu Glu Gln Thr Glu Arg
1685 1690 1695

Ala Arg Lys Leu Ala Glu Gln Glu Leu Leu Asp Ser Asn Glu Arg
1700 1705 1710

- 139 -

Val	Gln	Leu	Leu	His	Thr	Gln	Asn	Thr	Ser	Leu	Ile	His	Thr	Lys
1715						1720					1725			
Lys	Lys	Leu	Glu	Thr	Asp	Leu	Met	Gln	Leu	Gln	Ser	Glu	Val	Glu
1730						1735					1740			
Asp	Ala	Ser	Arg	Asp	Ala	Arg	Asn	Ala	Glu	Glu	Lys	Ala	Lys	Lys
1745						1750					1755			
Ala	Ile	Thr	Asp	Ala	Ala	Met	Met	Ala	Glu	Glu	Leu	Lys	Lys	Glu
1760						1765					1770			
Gln	Asp	Thr	Ser	Ala	His	Leu	Glu	Arg	Met	Lys	Lys	Asn	Leu	Glu
1775						1780					1785			
Gln	Thr	Val	Lys	Asp	Leu	Gln	His	Arg	Leu	Asp	Glu	Ala	Glu	Gln
1790						1795					1800			
Leu	Ala	Leu	Lys	Gly	Gly	Lys	Lys	Gln	Ile	Gln	Lys	Leu	Glu	Thr
1805						1810					1815			
Arg	Ile	Arg	Glu	Leu	Glu	Phe	Glu	Leu	Glu	Gly	Glu	Gln	Lys	Lys
1820						1825					1830			
Asn	Thr	Glu	Ser	Val	Lys	Gly	Leu	Arg	Lys	Tyr	Glu	Arg	Arg	Val
1835						1840					1845			
Lys	Glu	Leu	Thr	Tyr	Gln	Ser	Glu	Glu	Asp	Arg	Lys	Asn	Val	Leu
1850						1855					1860			
Arg	Leu	Gln	Asp	Leu	Val	Asp	Lys	Leu	Gln	Val	Lys	Val	Lys	Ser
1865						1870					1875			
Tyr	Lys	Arg	Gln	Ala	Glu	Glu	Ala	Asp	Glu	Gln	Ala	Asn	Ala	His
1880						1885					1890			
Leu	Thr	Lys	Phe	Arg	Lys	Ala	Gln	His	Glu	Leu	Glu	Glu	Ala	Glu
1895						1900					1905			
Glu	Arg	Ala	Asp	Ile	Ala	Glu	Ser	Gln	Val	Asn	Lys	Leu	Arg	Ala
1910						1915					1920			
Lys	Thr	Arg	Asp	Phe	Thr	Ser	Ser	Arg	Met	Val	Val	His	Glu	Ser
1925						1930					1935			

- 140 -

Glu Glu
1940

<210> 81

<211> 943

<212> PRT

<213> Homo sapiens

<400> 81

Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val
1 5 10 15

Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly
20 25 30

Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
35 40 45

Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
50 55 60

Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65 70 75 80

Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
85 90 95

Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
100 105 110

Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
115 120 125

Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
130 135 140

Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145 150 155 160

Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu

- 141 -

165							170							175						
Tyr	Ile	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys					
			180						185				190							
Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys					
			195						200				205							
Gly	Pro	Cys	Pro	Gln	Glu	Asn	Cys	Ile	Ile	Ser	Lys	Leu	Phe	Lys	Glu					
			210			215					220									
Gly	Cys	Thr	Phe	Ile	Tyr	Asn	Ser	Thr	Gln	Asn	Ala	Thr	Ala	Ser	Ile					
					230					235					240					
Met	Phe	Met	Gln	Ser	Leu	Ser	Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser					
				245					250					255						
Thr	His	Asn	Gln	Glu	Ala	Pro	Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu					
			260						265					270						
Arg	Ser	Ala	Trp	Asp	Val	Ile	Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser					
			275						280				285							
Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu					
			290			295					300									
Val	Gln	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser					
			305		310					315				320						
Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu					
				325					330					335						
Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala					
			340						345				350							
Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn					
		355						360				365								
Ser	Asn	Asp	Asp	Arg	Lys	Leu	Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val					
		370				375					380									
Ser	Ala	Lys	Thr	Asp	Ile	Ser	Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe					
					390					395					400					

- 142 -

Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415

Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
 420 425 430

Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445

Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460

Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480

Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495

Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510

Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525

Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
 530 535 540

Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
 545 550 555 560

Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 565 570 575

Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
 580 585 590

Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
 595 600 605

Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
 610 615 620

Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
 625 630 635 640

- 143 -

Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
 645 650 655

Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
 660 665 670

Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
 675 680 685

Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
 690 695 700

Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
 705 710 715 720

Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
 725 730 735

Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val
 740 745 750

Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
 755 760 765

Ile Ile Asp Leu Glu Ala Val Lys Val Glu Glu Glu Leu Thr Leu Ser
 770 775 780

Trp Thr Ala Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr
 785 790 795 800

Glu Ile Arg Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn
 805 810 815

Asn Ala Ile Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly
 820 825 830

Ile Arg Glu Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro
 835 840 845

Glu His Gln Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val
 850 855 860

Ala Ile Arg Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn
 865 870 875 880

- 144 -

Ile Ala Gln Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro
 885 890 895

Ala Arg Asp Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu
 900 905 910

Ile Gly Ile Ile Cys Leu Ile Ile Val Val Thr His His Thr Leu Ser
 915 920 925

Arg Lys Lys Arg Ala Asp Lys Lys Glu Asn Gly Thr Lys Leu Leu
 930 935 940

<210> 82

<211> 294

<212> PRT

<213> Homo sapiens

<400> 82

Met Gln Pro Glu Gly Ala Glu Lys Gly Lys Ser Phe Lys Gln Arg Leu
 1 5 10 15

Val Leu Lys Ser Ser Leu Ala Lys Glu Thr Leu Ser Glu Phe Leu Gly
 20 25 30

Thr Phe Ile Leu Ile Val Leu Gly Cys Gly Cys Val Ala Gln Ala Ile
 35 40 45

Leu Ser Arg Gly Arg Phe Gly Gly Val Ile Thr Ile Asn Val Gly Phe
 50 55 60

Ser Met Ala Val Ala Met Ala Ile Tyr Val Ala Gly Gly Val Ser Gly
 65 70 75 80

Gly His Ile Asn Pro Ala Val Ser Leu Ala Met Cys Leu Phe Gly Arg
 85 90 95

Met Lys Trp Phe Lys Leu Pro Phe Tyr Val Gly Ala Gln Phe Leu Gly
 100 105 110

Ala Phe Val Gly Ala Ala Thr Val Phe Gly Ile Tyr Tyr Asp Gly Leu

- 145 -

115					120					125					
Met	Ser	Phe	Ala	Gly	Gly	Lys	Leu	Leu	Ile	Val	Gly	Glu	Asn	Ala	Thr
	130					135					140				
Ala	His	Ile	Phe	Ala	Thr	Tyr	Pro	Ala	Pro	Tyr	Leu	Ser	Leu	Ala	Asn
145					150					155					160
Ala	Phe	Ala	Asp	Gln	Val	Val	Ala	Thr	Met	Ile	Leu	Leu	Ile	Ile	Val
				165					170					175	
Phe	Ala	Ile	Phe	Asp	Ser	Arg	Asn	Leu	Gly	Ala	Pro	Arg	Gly	Leu	Glu
			180					185					190		
Pro	Ile	Ala	Ile	Gly	Leu	Leu	Ile	Ile	Val	Ile	Ala	Ser	Ser	Leu	Gly
		195					200					205			
Leu	Asn	Ser	Gly	Cys	Ala	Met	Asn	Pro	Ala	Arg	Asp	Leu	Ser	Pro	Arg
	210					215					220				
Leu	Phe	Thr	Ala	Leu	Ala	Gly	Trp	Gly	Phe	Glu	Val	Phe	Arg	Ala	Gly
225					230					235					240
Asn	Asn	Phe	Trp	Trp	Ile	Pro	Val	Val	Gly	Pro	Leu	Val	Gly	Ala	Val
			245						250					255	
Ile	Gly	Gly	Leu	Ile	Tyr	Val	Leu	Val	Ile	Glu	Ile	His	His	Pro	Glu
			260					265					270		
Pro	Asp	Ser	Val	Phe	Lys	Ala	Glu	Gln	Ser	Glu	Asp	Lys	Pro	Glu	Lys
	275						280					285			
Tyr	Glu	Leu	Ser	Val	Ile										
	290														
<210> 83															
<211> 292															
<212> PRT															
<213> Homo sapiens															
<400> 83															

- 146 -

Met Gly Arg Gln Lys Glu Leu Val Ser Arg Cys Gly Glu Met Leu His
1 5 10 15

Ile Arg Tyr Arg Leu Leu Arg Gln Ala Leu Ala Glu Cys Leu Gly Thr
20 25 30

Leu Ile Leu Val Met Phe Gly Cys Gly Ser Val Ala Gln Val Val Leu
35 40 45

Ser Arg Gly Thr His Gly Gly Phe Leu Thr Ile Asn Leu Ala Phe Gly
50 55 60

Phe Ala Val Thr Leu Gly Ile Leu Ile Ala Gly Gln Val Ser Gly Ala
65 70 75 80

His Leu Asn Pro Ala Val Thr Phe Ala Met Cys Phe Leu Ala Arg Glu
85 90 95

Pro Trp Ile Lys Leu Pro Ile Tyr Thr Leu Ala Gln Thr Leu Gly Ala
100 105 110

Phe Leu Gly Ala Gly Ile Val Phe Gly Leu Tyr Tyr Asp Ala Ile Trp
115 120 125

His Phe Ala Asp Asn Gln Leu Phe Val Ser Gly Pro Asn Gly Thr Ala
130 135 140

Gly Ile Phe Ala Thr Tyr Pro Ser Gly His Leu Asp Met Ile Asn Gly
145 150 155 160

Phe Phe Asp Gln Phe Ile Gly Thr Ala Ser Leu Ile Val Cys Val Leu
165 170 175

Ala Ile Val Asp Pro Tyr Asn Asn Pro Val Pro Arg Gly Leu Glu Ala
180 185 190

Phe Thr Val Gly Leu Val Val Leu Val Ile Gly Thr Ser Met Gly Phe
195 200 205

Asn Ser Gly Tyr Ala Val Asn Pro Ala Arg Asp Phe Gly Pro Arg Leu
210 215 220

Phe Thr Ala Leu Ala Gly Trp Gly Ser Ala Val Phe Thr Thr Gly Gln
225 230 235 240

- 147 -

His Trp Trp Trp Val Pro Ile Val Ser Pro Leu Leu Gly Ser Ile Ala
245 250 255

Gly Val Phe Val Tyr Gln Leu Met Ile Gly Cys His Leu Glu Gln Pro
260 265 270

Pro Pro Ser Asn Glu Glu Glu Asn Val Lys Leu Ala His Val Lys His
275 280 285

Lys Glu Gln Ile
290

<210> 84

<211> 283

<212> PRT

<213> Homo sapiens

<400> 84

Met Ala Val Pro Pro Thr Tyr Ala Asp Leu Gly Lys Ser Ala Arg Asp
1 5 10 15

Val Phe Thr Lys Gly Tyr Gly Phe Gly Leu Ile Lys Leu Asp Leu Lys
20 25 30

Thr Lys Ser Glu Asn Gly Leu Glu Phe Thr Ser Ser Gly Ser Ala Asn
35 40 45

Thr Glu Thr Thr Lys Val Thr Gly Ser Leu Glu Thr Lys Tyr Arg Trp
50 55 60

Thr Glu Tyr Gly Leu Thr Phe Thr Glu Lys Trp Asn Thr Asp Asn Thr
65 70 75 80

Leu Gly Thr Glu Ile Thr Val Glu Asp Gln Leu Ala Arg Gly Leu Lys
85 90 95

Leu Thr Phe Asp Ser Ser Phe Ser Pro Asn Thr Gly Lys Lys Asn Ala
100 105 110

Lys Ile Lys Thr Gly Tyr Lys Arg Glu His Ile Asn Leu Gly Cys Asp
115 120 125

- 148 -

Met Asp Phe Asp Ile Ala Gly Pro Ser Ile Arg Gly Ala Leu Val Leu
 130 135 140

Gly Tyr Glu Gly Trp Leu Ala Gly Tyr Gln Met Asn Phe Glu Thr Ala
 145 150 155 160

Lys Ser Arg Val Thr Gln Ser Asn Phe Ala Val Gly Tyr Lys Thr Asp
 165 170 175

Glu Phe Gln Leu His Thr Asn Val Asn Asp Gly Thr Glu Phe Gly Gly
 180 185 190

Ser Ile Tyr Gln Lys Val Asn Lys Lys Leu Glu Thr Ala Val Asn Leu
 195 200 205

Ala Trp Thr Ala Gly Asn Ser Asn Thr Arg Phe Gly Ile Ala Ala Lys
 210 215 220

Tyr Gln Ile Asp Pro Asp Ala Cys Phe Ser Ala Lys Val Asn Asn Ser
 225 230 235 240

Ser Leu Ile Gly Leu Gly Tyr Thr Gln Thr Leu Lys Pro Gly Ile Lys
 245 250 255

Leu Thr Leu Ser Ala Leu Leu Asp Gly Lys Asn Val Asn Ala Gly Gly
 260 265 270

His Lys Leu Gly Leu Gly Leu Glu Phe Gln Ala
 275 280

<210> 85

<211> 195

<212> PRT

<213> Homo sapiens

<400> 85

Met Gly Ser Arg Ala Ser Thr Leu Leu Arg Asp Glu Glu Leu Glu Glu
 1 5 10 15

- 149 -

Ile Lys Lys Glu Thr Gly Phe Ser His Ser Gln Ile Thr Arg Leu Tyr
 20 25 30

Ser Arg Phe Thr Ser Leu Asp Lys Gly Glu Asn Gly Thr Leu Ser Arg
 35 40 45

Glu Asp Phe Gln Arg Ile Pro Glu Leu Ala Ile Asn Pro Leu Gly Asp
 50 55 60

Arg Ile Ile Asn Ala Phe Phe Pro Glu Gly Glu Asp Gln Val Asn Phe
 65 70 75 80

Arg Gly Phe Met Arg Thr Leu Ala His Phe Arg Pro Ile Glu Asp Asn
 85 90 95

Glu Lys Ser Lys Asp Val Asn Gly Pro Glu Pro Leu Asn Ser Arg Ser
 100 105 110

Asn Lys Leu His Phe Ala Phe Arg Leu Tyr Asp Leu Asp Lys Asp Glu
 115 120 125

Lys Ile Ser Arg Asp Glu Leu Leu Gln Val Leu Arg Met Met Val Gly
 130 135 140

Val Asn Ile Ser Asp Glu Gln Leu Gly Ser Ile Ala Asp Arg Thr Ile
 145 150 155 160

Gln Glu Ala Asp Gln Asp Gly Asp Ser Ala Ile Ser Phe Thr Glu Phe
 165 170 175

Val Lys Val Leu Glu Lys Val Asp Val Glu Gln Lys Met Ser Ile Arg
 180 185 190

Phe Leu His
 195

<210> 86

<211> 535

<212> PRT

<213> Homo sapiens

<400> 86

- 150 -

Met Ala Ser Leu Ser Leu Ala Pro Val Asn Ile Phe Lys Ala Gly Ala
 1 5 10 15
 Asp Glu Glu Arg Ala Glu Thr Ala Arg Leu Thr Ser Phe Ile Gly Ala
 20 25 30
 Ile Ala Ile Gly Asp Leu Val Lys Ser Thr Leu Gly Pro Lys Gly Met
 35 40 45
 Asp Lys Ile Leu Leu Ser Ser Gly Arg Asp Ala Ser Leu Met Val Thr
 50 55 60
 Asn Asp Gly Ala Thr Ile Leu Lys Asn Ile Gly Val Asp Asn Pro Ala
 65 70 75 80
 Ala Lys Val Leu Val Asp Met Ser Arg Val Gln Asp Asp Glu Val Gly
 85 90 95
 Asp Gly Thr Thr Ser Val Thr Val Leu Ala Ala Glu Leu Leu Arg Glu
 100 105 110
 Ala Glu Ser Leu Ile Ala Lys Lys Ile His Pro Gln Thr Ile Ile Ala
 115 120 125
 Gly Trp Arg Glu Ala Thr Lys Ala Ala Arg Glu Ala Leu Leu Ser Ser
 130 135 140
 Ala Val Asp His Gly Ser Asp Glu Val Lys Phe Arg Gln Asp Leu Met
 145 150 155 160
 Asn Ile Ala Gly Thr Thr Leu Ser Ser Lys Leu Leu Thr His His Lys
 165 170 175
 Asp His Phe Thr Lys Leu Ala Val Glu Ala Val Leu Arg Leu Lys Gly
 180 185 190
 Ser Gly Asn Leu Glu Ala Ile His Ile Ile Lys Lys Leu Gly Gly Ser
 195 200 205
 Leu Ala Asp Ser Tyr Leu Asp Glu Gly Phe Leu Leu Asp Lys Lys Ile
 210 215 220
 Gly Val Asn Gln Pro Lys Arg Ile Glu Asn Ala Lys Ile Leu Ile Ala
 225 230 235 240

- 151 -

Asn Thr Gly Met Asp Thr Asp Lys Ile Lys Ile Phe Gly Ser Arg Val
245 250 255

Arg Val Asp Ser Thr Ala Lys Val Ala Glu Ile Glu His Ala Glu Lys
260 265 270

Glu Lys Met Lys Glu Lys Val Glu Arg Ile Leu Lys His Gly Ile Asn
275 280 285

Cys Phe Ile Asn Arg Gln Leu Ile Tyr Asn Tyr Pro Glu Gln Leu Phe
290 295 300

Gly Ala Ala Gly Val Met Ala Ile Glu His Ala Asp Phe Ala Gly Val
305 310 315 320

Glu Arg Leu Ala Leu Val Thr Gly Gly Glu Ile Ala Ser Thr Phe Asp
325 330 335

His Pro Glu Leu Val Lys Leu Gly Ser Cys Lys Leu Ile Glu Glu Val
340 345 350

Met Ile Gly Glu Asp Lys Leu Ile His Phe Ser Gly Val Ala Leu Gly
355 360 365

Glu Ala Cys Thr Ile Val Leu Arg Gly Ala Thr Gln Gln Ile Leu Asp
370 375 380

Glu Ala Glu Arg Ser Leu His Asp Ala Leu Cys Val Leu Ala Gln Thr
385 390 395 400

Val Lys Asp Ser Arg Thr Val Tyr Gly Gly Gly Cys Ser Glu Met Leu
405 410 415

Met Ala His Ala Val Thr Gln Leu Ala Asn Arg Thr Pro Gly Lys Glu
420 425 430

Ala Val Ala Met Glu Ser Tyr Ala Lys Ala Leu Arg Met Leu Pro Thr
435 440 445

Ile Ile Ala Asp Asn Ala Gly Tyr Asp Ser Ala Asp Leu Val Ala Gln
450 455 460

- 152 -

Leu Arg Ala Ala His Ser Glu Gly Asn Thr Thr Ala Gly Leu Asp Met
465 470 475 480

Arg Glu Gly Thr Ile Gly Asp Met Ala Ile Leu Gly Ile Thr Glu Ser
485 490 495

Phe Gln Val Lys Arg Gln Val Leu Leu Ser Ala Ala Glu Ala Ala Glu
500 505 510

Val Ile Leu Arg Val Asp Asn Ile Ile Lys Ala Ala Pro Arg Lys Arg
515 520 525

Val Pro Asp His His Pro Cys
530 535

<210> 87

<211> 447

<212> PRT

<213> Homo sapiens

<400> 87

Met Ser Leu Trp Leu Gly Ala Pro Val Pro Asp Ile Pro Pro Asp Ser
1 5 10 15

Ala Val Glu Leu Trp Lys Pro Gly Ala Gln Asp Ala Ser Ser Gln Ala
20 25 30

Gln Gly Gly Ser Ser Cys Ile Leu Arg Glu Glu Ala Arg Met Pro His
35 40 45

Ser Ala Gly Gly Thr Ala Gly Val Gly Leu Glu Ala Ala Glu Pro Thr
50 55 60

Ala Leu Leu Thr Arg Ala Glu Pro Pro Ser Glu Pro Thr Glu Ile Arg
65 70 75 80

Pro Gln Lys Arg Lys Lys Gly Pro Ala Pro Lys Met Leu Gly Asn Glu
85 90 95

Leu Cys Ser Val Cys Gly Asp Lys Ala Ser Gly Phe His Tyr Asn Val
100 105 110

- 153 -

Leu Ser Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Val Ile Lys
 115 120 125

Gly Ala His Tyr Ile Cys His Ser Gly Gly His Cys Pro Met Asp Thr
 130 135 140

Tyr Met Arg Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Arg Gln
 145 150 155 160

Ala Gly Met Arg Glu Glu Cys Val Leu Ser Glu Glu Gln Ile Arg Leu
 165 170 175

Lys Lys Leu Lys Arg Gln Glu Glu Glu Gln Ala His Ala Thr Ser Leu
 180 185 190

Pro Pro Arg Arg Ser Ser Pro Pro Gln Ile Leu Pro Gln Leu Ser Pro
 195 200 205

Glu Gln Leu Gly Met Ile Glu Lys Leu Val Ala Ala Gln Gln Gln Cys
 210 215 220

Asn Arg Arg Ser Phe Ser Asp Arg Leu Arg Val Thr Pro Trp Pro Met
 225 230 235 240

Ala Pro Asp Pro His Ser Arg Glu Ala Arg Gln Gln Arg Phe Ala His
 245 250 255

Phe Thr Glu Leu Ala Ile Val Ser Val Gln Glu Ile Val Asp Phe Ala
 260 265 270

Lys Gln Leu Pro Gly Phe Leu Gln Leu Ser Arg Glu Asp Gln Ile Ala
 275 280 285

Leu Leu Lys Thr Ser Ala Ile Glu Val Met Leu Leu Glu Thr Ser Arg
 290 295 300

Arg Tyr Asn Pro Gly Ser Glu Ser Ile Thr Phe Leu Lys Asp Phe Ser
 305 310 315 320

Tyr Asn Arg Glu Asp Phe Ala Lys Ala Gly Leu Gln Val Glu Phe Ile
 325 330 335

Asn Pro Ile Phe Glu Phe Ser Arg Ala Met Asn Glu Leu Gln Leu Asn
 340 345 350

- 154 -

Asp Ala Glu Phe Ala Leu Leu Ile Ala Ile Ser Ile Phe Ser Ala Asp
 355 360 365

Arg Pro Asn Val Gln Asp Gln Leu Gln Val Glu Arg Leu Gln His Thr
 370 375 380

Tyr Val Glu Ala Leu His Ala Tyr Val Ser Ile His His Pro His Asp
 385 390 395 400

Arg Leu Met Phe Pro Arg Met Leu Met Lys Leu Val Ser Leu Arg Thr
 405 410 415

Leu Ser Ser Val His Ser Glu Gln Val Phe Ala Leu Arg Leu Gln Asp
 420 425 430

Lys Lys Leu Pro Pro Leu Leu Ser Glu Ile Trp Asp Val His Glu
 435 440 445

<210> 88

<211> 826

<212> PRT

<213> Homo sapiens

<400> 88

Met Glu Gly Ala Gly Gly Ala Asn Asp Lys Lys Lys Ile Ser Ser Glu
 1 5 10 15

Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys
 20 25 30

Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His
 35 40 45

Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile
 50 55 60

Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile
 65 70 75 80

- 155 -

Glu Asp Asp Met Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu
 85 90 95

Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile
 100 105 110

Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr
 115 120 125

Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met
 130 135 140

Arg Glu Met Leu Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu
 145 150 155 160

Gln Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr
 165 170 175

Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
 180 185 190

His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
 195 200 205

Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys
 210 215 220

Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys
 225 230 235 240

Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp
 245 250 255

Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly
 260 265 270

Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr
 275 280 285

Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln
 290 295 300

Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln
 305 310 315 320

- 156 -

Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val
325 330 335

Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe
340 345 350

Ser Leu Gln Gln Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp
355 360 365

Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser
370 375 380

Ser Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu
385 390 395 400

Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn
405 410 415

Asp Thr Glu Thr Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn
420 425 430

Asp Val Met Leu Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu
435 440 445

Ala Met Ser Pro Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser
450 455 460

Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro
465 470 475 480

Asn Pro Glu Ser Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp
485 490 495

Gln Thr Pro Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu
500 505 510

Pro Asn Ser Pro Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val
515 520 525

Asn Glu Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr
530 535 540

Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu
545 550 555 560

- 157 -

Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser
565 570 575

Phe Asp Gln Leu Ser Pro Leu Glu Ser Ser Ser Ala Ser Pro Glu Ser
580 585 590

Ala Ser Pro Gln Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln
595 600 605

Glu Pro Thr Ala Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu
610 615 620

Lys Thr Val Thr Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala
625 630 635 640

Ser Pro Ser Pro Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser
645 650 655

Ser Pro Tyr Arg Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala
660 665 670

Gly Lys Gly Val Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro
675 680 685

Asn Val Leu Ser Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu
690 695 700

Glu Leu Asn Pro Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg
705 710 715 720

Lys Met Glu His Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr
725 730 735

Leu Leu Gln Gln Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp
740 745 750

Lys Arg Val Lys Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln
755 760 765

Lys Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly
770 775 780

- 158 -

Gln Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys
785 790 795 800

Glu Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu
805 810 815

Glu Leu Leu Arg Ala Leu Asp Gln Val Asn
820 825

<210> 89

<211> 1575

<212> PRT

<213> Homo sapiens

<400> 89

Met Pro His Glu Glu Leu Pro Ser Leu Gln Arg Pro Arg Tyr Gly Ser
1 5 10 15

Ile Val Asp Asp Glu Arg Leu Ser Ala Glu Glu Met Asp Glu Arg Arg
20 25 30

Arg Gln Asn Ile Ala Tyr Glu Tyr Leu Cys His Leu Glu Glu Ala Lys
35 40 45

Arg Trp Met Glu Val Cys Leu Val Glu Glu Leu Pro Pro Thr Thr Glu
50 55 60

Leu Glu Glu Gly Leu Arg Asn Gly Val Tyr Leu Ala Lys Leu Ala Lys
65 70 75 80

Phe Phe Ala Pro Lys Met Val Ser Glu Lys Lys Ile Tyr Asp Val Glu
85 90 95

Gln Thr Arg Tyr Lys Lys Ser Gly Leu His Phe Arg His Thr Asp Asn
100 105 110

Thr Val Gln Trp Leu Arg Ala Met Glu Ser Ile Gly Leu Pro Lys Ile
115 120 125

Phe Tyr Pro Glu Thr Thr Asp Val Tyr Asp Arg Lys Asn Ile Pro Arg
130 135 140

- 159 -

Met Ile Tyr Cys Ile His Ala Leu Ser Leu Tyr Leu Phe Lys Leu Gly
 145 150 155 160

Ile Ala Pro Gln Ile Gln Asp Leu Leu Gly Lys Val Asp Phe Thr Glu
 165 170 175

Glu Glu Ile Ser Asn Met Arg Lys Glu Leu Glu Lys Tyr Gly Ile Gln
 180 185 190

Met Pro Ser Phe Ser Lys Ile Gly Gly Ile Leu Ala Asn Glu Leu Ser
 195 200 205

Val Asp Glu Ala Ala Leu His Ala Ala Val Ile Ala Ile Asn Glu Ala
 210 215 220

Val Glu Lys Gly Ile Ala Glu Gln Thr Val Val Thr Leu Arg Asn Pro
 225 230 235 240

Asn Ala Val Leu Thr Leu Val Asp Asp Asn Leu Ala Pro Glu Tyr Gln
 245 250 255

Lys Glu Leu Trp Asp Ala Lys Lys Lys Lys Glu Glu Asn Ala Arg Leu
 260 265 270

Lys Asn Ser Cys Ile Ser Glu Glu Glu Arg Asp Ala Tyr Glu Glu Leu
 275 280 285

Leu Thr Gln Ala Glu Ile Gln Gly Asn Ile Asn Lys Val Asn Arg Gln
 290 295 300

Ala Ala Val Asp His Ile Asn Ala Val Ile Pro Glu Gly Asp Pro Glu
 305 310 315 320

Asn Thr Leu Leu Ala Leu Lys Lys Pro Glu Ala Gln Leu Pro Ala Val
 325 330 335

Tyr Pro Phe Ala Ala Ala Met Tyr Gln Asn Glu Leu Phe Asn Leu Gln
 340 345 350

Lys Gln Asn Thr Met Asn Tyr Leu Ala His Glu Glu Leu Leu Ile Ala
 355 360 365

Val Glu Met Leu Ser Ala Val Ala Leu Leu Asn Gln Ala Leu Glu Ser
 370 375 380

- 160 -

Asn Asp Leu Val Ser Val Gln Asn Gln Leu Arg Ser Pro Ala Ile Gly
385 390 395 400

Leu Asn Asn Leu Asp Lys Ala Tyr Val Glu Arg Tyr Ala Asn Thr Leu
405 410 415

Leu Ser Val Lys Leu Glu Val Leu Ser Gln Gly Gln Asp Asn Leu Ser
420 425 430

Trp Asn Glu Ile Gln Asn Cys Ile Asp Met Val Asn Ala Gln Ile Gln
435 440 445

Glu Glu Asn Asp Arg Val Val Ala Val Gly Tyr Ile Asn Glu Ala Ile
450 455 460

Asp Glu Gly Asn Pro Leu Arg Thr Leu Glu Thr Leu Leu Leu Pro Thr
465 470 475 480

Ala Asn Ile Ser Asp Val Asp Pro Ala His Ala Gln His Tyr Gln Asp
485 490 495

Val Leu Tyr His Ala Lys Ser Gln Lys Leu Gly Asp Ser Glu Ser Val
500 505 510

Ser Lys Val Leu Trp Leu Asp Glu Ile Gln Gln Ala Val Asp Glu Ala
515 520 525

Asn Val Asp Glu Asp Arg Ala Lys Gln Trp Val Thr Leu Val Val Asp
530 535 540

Val Asn Gln Cys Leu Glu Gly Lys Lys Ser Ser Asp Ile Leu Ser Val
545 550 555 560

Leu Lys Ser Ser Thr Ser Asn Ala Asn Asp Ile Ile Pro Glu Cys Ala
565 570 575

Asp Lys Tyr Tyr Asp Ala Leu Val Lys Ala Lys Glu Leu Lys Ser Glu
580 585 590

Arg Val Ser Ser Asp Gly Ser Trp Leu Lys Leu Asn Leu His Lys Lys
595 600 605

Tyr Asp Tyr Tyr Tyr Asn Thr Asp Ser Lys Glu Ser Ser Trp Val Thr

610

620

Gly Leu Leu Val Lys Asn Arg Ile Thr Leu Glu Asp Val Ile Ser His
835 840 845

- 162 -

Ser Lys Lys Leu Asn Lys Lys Lys Gly Gly Glu Met Glu Ile Leu Asn
850 855 860

Asn Thr Asp Asn Gln Gly Ile Lys Ser Leu Ser Lys Glu Arg Arg Lys
865 870 875 880

Thr Leu Glu Thr Tyr Gln Gln Leu Phe Tyr Leu Leu Gln Thr Asn Pro
885 890 895

Leu Tyr Leu Ala Lys Leu Ile Phe Gln Met Pro Gln Asn Lys Ser Thr
900 905 910

Lys Phe Met Asp Thr Val Ile Phe Thr Leu Tyr Asn Tyr Ala Ser Asn
915 920 925

Gln Arg Glu Glu Tyr Leu Leu Leu Lys Leu Phe Lys Thr Ala Leu Glu
930 935 940

Glu Glu Ile Lys Ser Lys Val Asp Gln Val Gln Asp Ile Val Thr Gly
945 950 955 960

Asn Pro Thr Val Ile Lys Met Val Val Ser Phe Asn Arg Gly Ala Arg
965 970 975

Gly Gln Asn Thr Leu Arg Gln Leu Leu Ala Pro Val Val Lys Glu Ile
980 985 990

Ile Asp Asp Lys Ser Leu Ile Ile Asn Thr Asn Pro Val Glu Val Tyr
995 1000 1005

Lys Ala Trp Val Asn Gln Leu Glu Thr Gln Thr Gly Glu Ala Ser
1010 1015 1020

Lys Leu Pro Tyr Asp Val Thr Thr Glu Gln Ala Leu Thr Tyr Pro
1025 1030 1035

Glu Val Lys Asn Lys Leu Glu Ala Ser Ile Glu Asn Leu Arg Arg
1040 1045 1050

Val Thr Asp Lys Val Leu Asn Ser Ile Ile Ser Ser Leu Asp Leu
1055 1060 1065

Leu Pro Tyr Gly Leu Arg Tyr Ile Ala Lys Val Leu Lys Asn Ser
1070 1075 1080

- 163 -

Ile	His	Glu	Lys	Phe	Pro	Asp	Ala	Thr	Glu	Asp	Glu	Leu	Leu	Lys
1085						1090					1095			
Ile	Val	Gly	Asn	Leu	Leu	Tyr	Tyr	Arg	Tyr	Met	Asn	Pro	Ala	Ile
1100						1105					1110			
Val	Ala	Pro	Asp	Gly	Phe	Asp	Ile	Ile	Asp	Met	Thr	Ala	Gly	Gly
1115						1120					1125			
Gln	Ile	Asn	Ser	Asp	Gln	Arg	Arg	Asn	Leu	Gly	Ser	Val	Ala	Lys
1130						1135					1140			
Val	Leu	Gln	His	Ala	Ala	Ser	Asn	Lys	Leu	Phe	Glu	Gly	Glu	Asn
1145						1150					1155			
Glu	His	Leu	Ser	Ser	Met	Asn	Asn	Tyr	Leu	Ser	Glu	Thr	Tyr	Gln
1160						1165					1170			
Glu	Phe	Arg	Lys	Tyr	Phe	Lys	Glu	Ala	Cys	Asn	Val	Pro	Glu	Pro
1175						1180					1185			
Glu	Glu	Lys	Phe	Asn	Met	Asp	Lys	Tyr	Thr	Asp	Leu	Val	Thr	Val
1190						1195					1200			
Ser	Lys	Pro	Val	Ile	Tyr	Ile	Ser	Ile	Glu	Glu	Ile	Ile	Ser	Thr
1205						1210					1215			
His	Ser	Leu	Leu	Leu	Glu	His	Gln	Asp	Ala	Ile	Ala	Pro	Glu	Lys
1220						1225					1230			
Asn	Asp	Leu	Leu	Ser	Glu	Leu	Leu	Gly	Ser	Leu	Gly	Glu	Val	Pro
1235						1240					1245			
Thr	Val	Glu	Ser	Phe	Leu	Gly	Glu	Gly	Ala	Val	Asp	Pro	Asn	Asp
1250						1255					1260			
Pro	Asn	Lys	Ala	Asn	Thr	Leu	Ser	Gln	Leu	Ser	Lys	Thr	Glu	Ile
1265						1270					1275			
Ser	Leu	Val	Leu	Thr	Ser	Lys	Tyr	Asp	Ile	Glu	Asp	Gly	Glu	Ala
1280						1285					1290			
Ile	Asp	Ser	Arg	Ser	Leu	Met	Ile	Lys	Thr	Lys	Lys	Leu	Ile	Ile
1295						1300					1305			

- 164 -

Asp Val Ile Arg Asn Gln Pro Gly Asn Thr Leu Thr Glu Ile Leu
1310 1315 1320

Glu Thr Pro Ala Thr Ala Gln Gln Glu Val Asp His Ala Thr Asp
1325 1330 1335

Met Val Ser Arg Ala Met Ile Asp Ser Arg Thr Pro Glu Glu Met
1340 1345 1350

Lys His Ser Gln Ser Met Ile Glu Asp Ala Gln Leu Pro Leu Glu
1355 1360 1365

Gln Lys Lys Arg Lys Ile Gln Arg Asn Leu Arg Thr Leu Glu Gln
1370 1375 1380

Thr Gly His Val Ser Ser Glu Asn Lys Tyr Gln Asp Ile Leu Asn
1385 1390 1395

Glu Ile Ala Lys Asp Ile Arg Asn Gln Arg Ile Tyr Arg Lys Leu
1400 1405 1410

Arg Lys Ala Glu Leu Ala Lys Leu Gln Gln Thr Leu Asn Ala Leu
1415 1420 1425

Asn Lys Lys Ala Ala Phe Tyr Glu Glu Gln Ile Asn Tyr Tyr Asp
1430 1435 1440

Thr Tyr Ile Lys Thr Cys Leu Asp Asn Leu Lys Arg Lys Asn Thr
1445 1450 1455

Arg Arg Ser Ile Lys Leu Asp Gly Lys Gly Glu Pro Lys Gly Ala
1460 1465 1470

Lys Arg Ala Lys Pro Val Lys Tyr Thr Ala Ala Lys Leu His Glu
1475 1480 1485

Lys Gly Val Leu Leu Asp Ile Asp Asp Leu Gln Thr Asn Gln Phe
1490 1495 1500

Lys Asn Val Thr Phe Asp Ile Ile Ala Thr Glu Asp Val Gly Ile
1505 1510 1515

- 165 -

Phe Asp Val Arg Ser Lys Phe Leu Gly Val Glu Met Glu Lys Val
 1520 1525 1530

Gln Leu Asn Ile Gln Asp Leu Leu Gln Met Gln Tyr Glu Gly Val
 1535 1540 1545

Ala Val Met Lys Met Phe Asp Lys Val Lys Val Asn Val Asn Leu
 1550 1555 1560

Leu Ile Tyr Leu Leu Asn Lys Lys Phe Tyr Gly Lys
 1565 1570 1575

<210> 90

<211> 713

<212> PRT

<213> Homo sapiens

<400> 90

Leu Ala Cys Phe Leu Asp Lys His His Asp Ile Ile Ile Ile Asp His
 1 5 10 15

Arg Asn Pro Arg Gln Leu Asp Ala Glu Ala Leu Cys Arg Ser Ile Arg
 20 25 30

Ser Ser Lys Leu Ser Glu Asn Thr Val Ile Val Gly Val Val Arg Arg
 35 40 45

Val Asp Arg Glu Glu Leu Ser Val Met Pro Phe Ile Ser Ala Gly Phe
 50 55 60

Thr Arg Arg Tyr Val Glu Asn Pro Asn Ile Met Ala Cys Tyr Asn Glu
 65 70 75 80

Leu Leu Gln Leu Glu Phe Gly Glu Val Arg Ser Gln Leu Lys Leu Arg
 85 90 95

Ala Cys Asn Ser Val Phe Thr Ala Leu Glu Asn Ser Glu Asp Ala Ile
 100 105 110

Glu Ile Thr Ser Glu Asp Arg Phe Ile Gln Tyr Ala Asn Pro Ala Phe
 115 120 125

- 166 -

Glu Thr Thr Met Gly Tyr Gln Ser Gly Glu Leu Ile Gly Lys Glu Leu
130 135 140

Gly Glu Val Pro Ile Asn Glu Lys Lys Ala Asp Leu Leu Asp Thr Ile
145 150 155 160

Asn Ser Cys Ile Arg Ile Gly Lys Glu Trp Gln Gly Ile Tyr Tyr Ala
165 170 175

Lys Lys Lys Asn Gly Asp Asn Ile Gln Gln Asn Val Lys Ile Ile Pro
180 185 190

Val Ile Gly Gln Gly Gly Lys Ile Arg His Tyr Val Ser Ile Ile Arg
195 200 205

Val Cys Asn Gly Asn Asn Lys Ala Glu Lys Ile Ser Glu Cys Val Gln
210 215 220

Ser Asp Thr Arg Thr Asp Asn Gln Thr Gly Lys His Lys Asp Arg Arg
225 230 235 240

Lys Gly Ser Leu Asp Val Lys Ala Val Ala Ser Arg Ala Thr Glu Val
245 250 255

Ser Ser Gln Arg Arg His Ser Ser Met Ala Arg Ile His Ser Met Thr
260 265 270

Ile Glu Ala Pro Ile Thr Lys Val Ile Asn Val Ile Asn Ala Ala Gln
275 280 285

Glu Ser Ser Pro Met Pro Val Thr Glu Ala Leu Asp Arg Val Leu Glu
290 295 300

Ile Leu Arg Thr Thr Glu Leu Tyr Ser Pro Gln Phe Gly Ala Lys Asp
305 310 315 320

Asp Asp Pro His Ala Asn Asp Leu Val Gly Gly Leu Met Ser Asp Gly
325 330 335

Leu Arg Arg Leu Ser Gly Asn Glu Tyr Val Leu Ser Thr Lys Asn Thr
340 345 350

Gln Met Val Ser Ser Asn Ile Ile Thr Pro Ile Ser Leu Asp Asp Val
355 360 365

- 167 -

Pro Pro Arg Ile Ala Arg Ala Met Glu Asn Glu Glu Tyr Trp Asp Phe
370 375 380

Asp Ile Phe Glu Leu Glu Ala Ala Thr His Asn Arg Pro Leu Ile Tyr
385 390 395 400

Leu Gly Leu Lys Met Phe Ala Arg Phe Gly Ile Cys Glu Phe Leu His
405 410 415

Cys Ser Glu Ser Thr Leu Arg Ser Trp Leu Gln Ile Ile Glu Ala Asn
420 425 430

Tyr His Ser Ser Asn Pro Tyr His Asn Ser Thr His Ser Ala Asp Val
435 440 445

Leu His Ala Thr Ala Tyr Phe Leu Ser Lys Glu Arg Ile Lys Glu Thr
450 455 460

Leu Asp Pro Ile Asp Glu Val Ala Ala Leu Ile Ala Ala Thr Ile His
465 470 475 480

Asp Val Asp His Pro Gly Arg Thr Asn Ser Phe Leu Cys Asn Ala Gly
485 490 495

Ser Glu Leu Ala Ile Leu Tyr Asn Asp Thr Ala Val Leu Glu Ser His
500 505 510

His Ala Ala Leu Ala Phe Gln Leu Thr Thr Gly Asp Asp Lys Cys Asn
515 520 525

Ile Phe Lys Asn Met Glu Arg Asn Asp Tyr Arg Thr Leu Arg Gln Gly
530 535 540

Ile Ile Asp Met Val Leu Ala Thr Glu Met Thr Lys His Phe Glu His
545 550 555 560

Val Asn Lys Phe Val Asn Ser Ile Asn Lys Pro Leu Ala Thr Leu Glu
565 570 575

Glu Asn Gly Glu Thr Asp Lys Asn Gln Glu Val Ile Asn Thr Met Leu
580 585 590

- 168 -

Arg Thr Pro Glu Asn Arg Thr Leu Ile Lys Arg Met Leu Ile Lys Cys
595 600 605

Ala Asp Val Ser Asn Pro Cys Arg Pro Leu Gln Tyr Cys Ile Glu Trp
610 615 620

Ala Ala Arg Ile Ser Glu Glu Tyr Phe Ser Gln Thr Asp Glu Glu Lys
625 630 635 640

Gln Gln Gly Leu Pro Val Val Met Pro Val Phe Asp Arg Asn Thr Cys
645 650 655

Ser Ile Pro Lys Ser Gln Ile Ser Phe Ile Asp Tyr Phe Ile Thr Asp
660 665 670

Met Phe Asp Ala Trp Asp Ala Phe Val Asp Leu Pro Asp Leu Met Gln
675 680 685

His Leu Asp Asn Asn Phe Lys Tyr Trp Lys Gly Leu Asp Glu Met Lys
690 695 700

Leu Arg Asn Leu Arg Pro Pro Pro Glu
705 710

<210> 91

<211> 323

<212> PRT

<213> Homo sapiens

<400> 91

Met Asp Met Trp Thr Ala Leu Leu Ile Leu Gln Ala Leu Leu Leu Pro
1 5 10 15

Ser Leu Ala Asp Gly Ala Thr Pro Ala Leu Arg Phe Val Ala Val Gly
20 25 30

Asp Trp Gly Gly Val Pro Asn Ala Pro Phe His Thr Gly Pro Glu Met
35 40 45

Ala Asn Ala Lys Glu Ile Ala Arg Thr Val Gln Ile Leu Gly Ala Asp
50 55 60

- 169 -

Phe Ile Leu Ser Leu Gly Asp Asn Phe Tyr Phe Thr Gly Val Gln Asp
65 70 75 80

Ile Asn Asp Lys Arg Phe Gln Glu Thr Phe Glu Asp Val Phe Ser Asp
85 90 95

Arg Ser Leu Arg Lys Val Pro Trp Tyr Val Leu Ala Gly Asn His Asp
100 105 110

His Leu Gly Asn Val Ser Ala Gln Ile Ala Tyr Ser Lys Ile Ser Lys
115 120 125

Arg Trp Asn Phe Pro Ser Pro Phe Tyr Arg Leu His Phe Lys Ile Pro
130 135 140

Gln Thr Asn Val Ser Val Ala Ile Phe Met Leu Asp Thr Val Thr Leu
145 150 155 160

Cys Gly Asn Ser Asp Asp Phe Leu Ser Gln Gln Pro Glu Arg Pro Arg
165 170 175

Leu Thr Ala Arg Thr Gln Leu Ser Trp Leu Lys Lys Gln Leu Ala Ala
180 185 190

Ala Arg Glu Asp Tyr Val Leu Val Ala Gly His Tyr Pro Val Trp Ser
195 200 205

Ile Ala Glu His Gly Pro Thr His Cys Leu Val Lys Gln Leu Arg Pro
210 215 220

Leu Leu Ala Thr Tyr Gly Val Thr Ala Tyr Leu Cys Gly His Asp His
225 230 235 240

Asn Leu Gln Tyr Leu Gln Asp Glu Asn Gly Val Gly Tyr Val Leu Ser
245 250 255

Gly Ala Gly Asn Phe Met Asp Pro Ser Lys Arg His Gln Arg Lys Val
260 265 270

Pro Asn Gly Tyr Leu Arg Phe His Tyr Gly Thr Glu Asp Ser Leu Gly
275 280 285

Gly Phe Ala Tyr Val Glu Ile Ser Ser Lys Glu Met Thr Val Thr Tyr
290 295 300

- 170 -

Ile Glu Ala Ser Gly Lys Ser Leu Phe Lys Thr Arg Leu Pro Arg Arg
305 310 315 320

Ala Arg Pro

<210> 92

<211> 669

<212> PRT

<213> Homo sapiens

<400> 92

Met Met Arg Leu Arg Gly Ser Gly Met Leu Arg Asp Leu Leu Leu Arg
1 5 10 15

Ser Pro Ala Gly Val Ser Ala Thr Leu Arg Arg Ala Gln Pro Leu Val
20 25 30

Thr Leu Cys Arg Arg Pro Arg Gly Gly Gly Arg Pro Ala Ala Gly Pro
35 40 45

Ala Ala Ala Ala Arg Leu His Pro Trp Trp Gly Gly Gly Gly Trp Pro
50 55 60

Ala Glu Pro Leu Ala Arg Gly Leu Ser Ser Ser Pro Ser Glu Ile Leu
65 70 75 80

Gln Glu Leu Gly Lys Gly Ser Thr His Pro Gln Pro Gly Val Ser Pro
85 90 95

Pro Ala Ala Pro Ala Ala Pro Gly Pro Lys Asp Gly Pro Gly Glu Thr
100 105 110

Asp Ala Phe Gly Asn Ser Glu Gly Lys Glu Leu Val Ala Ser Gly Glu
115 120 125

Asn Lys Ile Lys Gln Gly Leu Leu Pro Ser Leu Glu Asp Leu Leu Phe
130 135 140

- 171 -

Tyr Thr Ile Ala Glu Gly Gln Glu Lys Ile Pro Val His Lys Phe Ile
145 150 155 160

Thr Ala Leu Lys Ser Thr Gly Leu Arg Thr Ser Asp Pro Arg Leu Lys
165 170 175

Glu Cys Met Asp Met Leu Arg Leu Thr Leu Gln Thr Thr Ser Asp Gly
180 185 190

Val Met Leu Asp Lys Asp Leu Phe Lys Lys Cys Val Gln Ser Asn Ile
195 200 205

Val Leu Leu Thr Gln Ala Phe Arg Arg Lys Phe Val-Ile Pro Asp Phe
210 215 220

Met Ser Phe Thr Ser His Ile Asp Glu Leu Tyr Glu Ser Ala Lys Lys
225 230 235 240

Gln Ser Gly Gly Lys Val Ala Asp Tyr Ile Pro Gln Leu Ala Lys Phe
245 250 255

Ser Pro Asp Leu Trp Gly Val Ser Val Cys Thr Val Asp Gly Gln Arg
260 265 270

His Ser Thr Gly Asp Thr Lys Val Pro Phe Cys Leu Gln Ser Cys Val
275 280 285

Lys Pro Leu Lys Tyr Ala Ile Ala Val Asn Asp Leu Gly Thr Glu Tyr
290 295 300

Val His Arg Tyr Val Gly Lys Glu Pro Ser Gly Leu Arg Phe Asn Lys
305 310 315 320

Leu Phe Leu Asn Glu Asp Asp Lys Pro His Asn Pro Met Val Asn Ala
325 330 335

Gly Ala Ile Val Val Thr Ser Leu Ile Lys Gln Gly Val Asn Asn Ala
340 345 350

Glu Lys Phe Asp Tyr Val Met Gln Phe Leu Asn Lys Met Ala Gly Asn
355 360 365

Glu Tyr Val Gly Phe Ser Asn Ala Thr Phe Gln Ser Glu Arg Glu Ser
370 375 380

- 172 -

Gly Asp Arg Asn Phe Ala Ile Gly Tyr Tyr Leu Lys Glu Lys Lys Cys
385 390 395 400

Phe Pro Glu Gly Thr Asp Met Val Gly Ile Leu Asp Phe Tyr Phe Gln
405 410 415

Leu Cys Ser Ile Glu Val Thr Cys Glu Ser Ala Ser Val Met Ala Ala
420 425 430

Thr Leu Ala Asn Gly Gly Phe Cys Pro Ile Thr Gly Glu Arg Val Leu
435 440 445

Ser Pro Glu Ala Val Arg Asn Thr Leu Ser Leu Met His Ser Cys Gly
450 455 460

Met Tyr Asp Phe Ser Gly Gln Phe Ala Phe His Val Gly Leu Pro Ala
465 470 475 480

Lys Ser Gly Val Ala Gly Gly Ile Leu Leu Val Val Pro Asn Val Met
485 490 495

Gly Met Met Cys Trp Ser Pro Pro Leu Asp Lys Met Gly Asn Ser Val
500 505 510

Lys Gly Ile His Phe Cys His Asp Leu Val Ser Leu Cys Asn Phe His
515 520 525

Asn Tyr Asp Asn Leu Arg His Phe Ala Lys Lys Leu Asp Pro Arg Arg
530 535 540

Glu Gly Gly Asp Gln Arg Val Lys Ser Val Ile Asn Leu Leu Phe Ala
545 550 555 560

Ala Tyr Thr Gly Asp Val Ser Ala Leu Arg Arg Phe Ala Leu Ser Ala
565 570 575

Met Asp Met Glu Gln Arg Asp Tyr Asp Ser Arg Thr Ala Leu His Val
580 585 590

Ala Ala Ala Glu Gly His Val Glu Val Val Lys Phe Leu Leu Glu Ala
595 600 605

Cys Lys Val Asn Pro Phe Pro Lys Asp Arg Trp Asn Asn Thr Pro Met
610 615 620

- 173 -

Asp Glu Ala Leu His Phe Gly His His Asp Val Phe Lys Ile Leu Gln
625 630 635 640

Glu Tyr Gln Val Gln Tyr Thr Pro Gln Gly Asp Ser Asp Asn Gly Lys
645 650 655

Glu Asn Gln Thr Val His Lys Asn Leu Asp Gly Leu Leu
660 665

<210> 93

<211> 383

<212> PRT

<213> Homo sapiens

<400> 93

Met Gly Val Lys Ala Ser Gln Thr Gly Phe Val Val Leu Val Leu Leu
1 5 10 15

Gln Cys Cys Ser Ala Tyr Lys Leu Val Cys Tyr Tyr Thr Ser Trp Ser
20 25 30

Gln Tyr Arg Glu Gly Asp Gly Ser Cys Phe Pro Asp Ala Leu Asp Arg
35 40 45

Phe Leu Cys Thr His Ile Ile Tyr Ser Phe Ala Asn Ile Ser Asn Asp
50 55 60

His Ile Asp Thr Trp Glu Trp Asn Asp Val Thr Leu Tyr Gly Met Leu
65 70 75 80

Asn Thr Leu Lys Asn Arg Asn Pro Asn Leu Lys Thr Leu Leu Ser Val
85 90 95

Gly Gly Trp Asn Phe Gly Ser Gln Arg Phe Ser Lys Ile Ala Ser Asn
100 105 110

Thr Gln Ser Arg Arg Thr Phe Ile Lys Ser Val Pro Pro Phe Leu Arg
115 120 125

- 174 -

Thr His Gly Phe Asp Gly Leu Asp Leu Ala Trp Leu Tyr Pro Gly Arg
 130 135 140

Arg Asp Lys Gln His Phe Thr Thr Leu Ile Lys Glu Met Lys Ala Glu
 145 150 155 160

Phe Ile Lys Glu Ala Gln Pro Gly Lys Lys Gln Leu Leu Leu Ser Ala
 165 170 175

Ala Leu Ser Ala Gly Lys Val Thr Ile Asp Ser Ser Tyr Asp Ile Ala
 180 185 190

Lys Ile Ser Gln His Leu Asp Phe Ile Ser Ile Met Thr Tyr Asp Phe
 195 200 205

His Gly Ala Trp Arg Gly Thr Thr Gly His His Ser Pro Leu Phe Arg
 210 215 220

Gly Gln Glu Asp Ala Ser Pro Asp Arg Phe Ser Asn Thr Asp Tyr Ala
 225 230 235 240

Val Gly Tyr Met Leu Arg Leu Gly Ala Pro Ala Ser Lys Leu Val Met
 245 250 255

Gly Ile Pro Thr Phe Gly Arg Ser Phe Thr Leu Ala Ser Ser Glu Thr
 260 265 270

Gly Val Gly Ala Pro Ile Ser Gly Pro Gly Ile Pro Gly Arg Phe Thr
 275 280 285

Lys Glu Ala Gly Thr Leu Ala Tyr Tyr Glu Ile Cys Asp Phe Leu Arg
 290 295 300

Gly Ala Thr Val His Arg Thr Leu Gly Gln Gln Val Pro Tyr Ala Thr
 305 310 315 320

Lys Gly Asn Gln Trp Val Gly Tyr Asp Asp Gln Glu Ser Val Lys Ser
 325 330 335

Lys Val Gln Tyr Leu Lys Asp Arg Gln Leu Ala Gly Ala Met Val Trp
 340 345 350

Ala Leu Asp Leu Asp Asp Phe Gln Gly Ser Phe Cys Gly Gln Asp Leu
 355 360 365

- 175 -

Arg Phe Pro Leu Thr Asn Ala Ile Lys Asp Ala Leu Ala Ala Thr
 370 375 380

<210> 94

<211> 433

<212> PRT

<213> Homo sapiens

<400> 94

Met Val Trp Lys Val Ala Val Phe Leu Ser Val Ala Leu Gly Ile Gly
 1 5 10 15

Ala Val Pro Ile Asp Asp Pro Glu Asp Gly Gly Lys His Trp Ala Val
 20 25 30

Ile Val Ala Gly Ser Asn Gly Trp Tyr Asn Tyr Arg His Gln Ala Asp
 35 40 45

Ala Cys His Ala Tyr Gln Ile Ile His Arg Asn Gly Ile Pro Asp Glu
 50 55 60

Gln Ile Val Val Met Met Tyr Asp Asp Ile Ala Tyr Ser Glu Asp Asn
 65 70 75 80

Pro Thr Pro Gly Ile Val Ile Asn Arg Pro Asn Gly Thr Asp Val Tyr
 85 90 95

Gln Gly Val Pro Lys Asp Tyr Thr Gly Glu Asp Val Thr Pro Gln Asn
 100 105 110

Phe Leu Ala Val Leu Arg Gly Asp Ala Glu Ala Val Lys Gly Ile Gly
 115 120 125

Ser Gly Lys Val Leu Lys Ser Gly Pro Gln Asp His Val Phe Ile Tyr
 130 135 140

Phe Thr Asp His Gly Ser Thr Gly Ile Leu Val Phe Pro Asn Glu Asp
 145 150 155 160

Leu His Val Lys Asp Leu Asn Glu Thr Ile His Tyr Met Tyr Lys His
 165 170 175

- 176 -

Lys Met Tyr Arg Lys Met Val Phe Tyr Ile Glu Ala Cys Glu Ser Gly
180 185 190

Ser Met Met Asn His Leu Pro Asp Asn Ile Asn Val Tyr Ala Thr Thr
195 200 205

Ala Ala Asn Pro Arg Glu Ser Ser Tyr Ala Cys Tyr Tyr Asp Glu Lys
210 215 220

Arg Ser Thr Tyr Leu Gly Asp Trp Tyr Ser Val Asn Trp Met Glu Asp
225 230 235 240

Ser Asp Val Glu Asp Leu Thr Lys Glu Thr Leu His Lys Gln Tyr His
245 250 255

Leu Val Lys Ser His Thr Asn Thr Ser His Val Met Gln Tyr Gly Asn
260 265 270

Lys Thr Ile Ser Thr Met Lys Val Met Gln Phe Gln Gly Met Lys Arg
275 280 285

Lys Ala Ser Ser Pro Val Pro Leu Pro Pro Val Thr His Leu Asp Leu
290 295 300

Thr Pro Ser Pro Asp Val Pro Leu Thr Ile Met Lys Arg Lys Leu Met
305 310 315 320

Asn Thr Asn Asp Leu Glu Glu Ser Arg Gln Leu Thr Glu Glu Ile Gln
325 330 335

Arg His Leu Asp Ala Arg His Leu Ile Glu Lys Ser Val Arg Lys Ile
340 345 350

Val Ser Leu Leu Ala Ala Ser Glu Ala Glu Val Glu Gln Leu Leu Ser
355 360 365

Glu Arg Ala Pro Leu Thr Gly His Ser Cys Tyr Pro Glu Ala Leu Leu
370 375 380

His Phe Arg Thr His Cys Phe Asn Trp His Ser Pro Thr Tyr Glu Tyr
385 390 395 400

- 177 -

Ala Leu Arg His Leu Tyr Val Leu Val Asn Leu Cys Glu Lys Pro Tyr
405 410 415

Pro Leu His Arg Ile Lys Leu Ser Met Asp His Val Cys Leu Gly His
420 425 430

Tyr

<210> 95

<211> 333

<212> PRT

<213> Homo sapiens

<400> 95

Met Asn Pro Thr Leu Ile Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser
1 5 10 15

Ala Thr Leu Thr Phe Asp His Ser Leu Glu Ala Gln Trp Thr Lys Trp
20 25 30

Lys Ala Met His Asn Arg Leu Tyr Gly Met Asn Glu Glu Gly Trp Arg
35 40 45

Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gln
50 55 60

Glu Tyr Arg Glu Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe
65 70 75 80

Gly Asp Met Thr Ser Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln
85 90 95

Asn Arg Lys Pro Arg Lys Gly Lys Val Phe Gln Glu Pro Leu Phe Tyr
100 105 110

Glu Ala Pro Arg Ser Val Asp Trp Arg Glu Lys Gly Tyr Val Thr Pro
115 120 125

Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr
130 135 140

- 178 -

Gly Ala Leu Glu Gly Gln Met Phe Arg Lys Thr Gly Arg Leu Ile Ser
 145 150 155 160

Leu Ser Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu
 165 170 175

Gly Cys Asn Gly Gly Leu Met Asp Tyr Ala Phe Gln Tyr Val Gln Asp
 180 185 190

Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu
 195 200 205

Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly
 210 215 220

Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala
 225 230 235 240

Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe
 245 250 255

Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu
 260 265 270

Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr
 275 280 285

Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu
 290 295 300

Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn
 305 310 315 320

His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val
 325 330

<210> 96

<211> 175

<212> PRT

<213> Homo sapiens

- 179 -

<400> 96

Met Thr Asp Cys Glu Phe Gly Tyr Ile Tyr Arg Leu Ala Gln Asp Tyr
1 5 10 15

Leu Gln Cys Val Leu Gln Ile Pro Gln Pro Gly Ser Gly Pro Ser Lys
20 25 30

Thr Ser Arg Val Leu Gln Asn Val Ala Phe Ser Val Gln Lys Glu Val
35 40 45

Glu Lys Asn Leu Lys Ser Cys Leu Asp Asn Val Asn Val Val Ser Val
50 55 60

Asp Thr Ala Arg Thr Leu Phe Asn Gln Val Met Glu Lys Glu Phe Glu
65 70 75 80

Asp Gly Ile Ile Asn Trp Gly Arg Ile Val Thr Ile Phe Ala Phe Glu
85 90 95

Gly Ile Leu Ile Lys Lys Leu Leu Arg Gln Gln Ile Ala Pro Asp Val
100 105 110

Asp Thr Tyr Lys Glu Ile Ser Tyr Phe Val Ala Glu Phe Ile Met Asn
115 120 125

Asn Thr Gly Glu Trp Ile Arg Gln Asn Gly Gly Trp Glu Asn Gly Phe
130 135 140

Val Lys Lys Phe Glu Pro Lys Ser Gly Trp Met Thr Phe Leu Glu Val
145 150 155 160

Thr Gly Lys Ile Cys Glu Met Leu Ser Leu Leu Lys Gln Tyr Cys
165 170 175

<210> 97

<211> 732

<212> PRT

<213> Homo sapiens

<400> 97

Met Thr Glu Gly Thr Cys Leu Arg Arg Arg Gly Gly Pro Tyr Lys Thr

- 180 -

1	5	10	15
Glu Pro Ala Thr Asp Leu Gly Arg Trp Arg Leu Asn Cys Glu Arg Gly	20	25	30
Arg Gln Thr Trp Thr Tyr Leu Gln Asp Glu Arg Ala Gly Arg Glu Gln	35	40	45
Thr Gly Leu Glu Ala Tyr Ala Leu Gly Leu Asp Thr Lys Asn Tyr Phe	50	55	60
Lys Asp Leu Pro Lys Ala His Thr Ala Phe Glu Gly Ala Leu Asn Gly	65	70	75
Met Thr Phe Tyr Val Gly Leu Gln Ala Glu Asp Gly His Trp Thr Gly	85	90	95
Asp Tyr Gly Gly Pro Leu Phe Leu Leu Pro Gly Leu Leu Ile Thr Cys	100	105	110
His Val Ala Arg Ile Pro Leu Pro Ala Gly Tyr Arg Glu Glu Ile Val	115	120	125
Arg Tyr Leu Arg Ser Val Gln Leu Pro Asp Gly Gly Trp Gly Leu His	130	135	140
Ile Glu Asp Lys Ser Thr Val Phe Gly Thr Ala Leu Asn Tyr Val Ser	145	150	155
Leu Arg Ile Leu Gly Val Gly Pro Asp Asp Pro Asp Leu Val Arg Ala	165	170	175
Arg Asn Ile Leu His Lys Lys Gly Gly Ala Val Ala Ile Pro Ser Trp	180	185	190
Gly Lys Phe Trp Leu Ala Val Leu Asn Val Tyr Ser Trp Glu Gly Leu	195	200	205
Asn Thr Leu Phe Pro Glu Met Trp Leu Phe Pro Asp Trp Ala Pro Ala	210	215	220
His Pro Ser Thr Leu Trp Cys His Cys Arg Gln Val Tyr Leu Pro Met	225	230	235
			240

- 181 -

Ser Tyr Cys Tyr Ala Val Arg Leu Ser Ala Ala Glu Asp Pro Leu Val
245 250 255

Gln Ser Leu Arg Gln Glu Leu Tyr Val Glu Asp Phe Ala Ser Ile Asp
260 265 270

Trp Leu Ala Gln Arg Asn Asn Val Ala Pro Asp Glu Leu Tyr Thr Pro
275 280 285

His Ser Trp Leu Leu Arg Val Val Tyr Ala Leu Leu Asn Leu Tyr Glu
290 295 300

His His His Ser Ala His Leu Arg Gln Arg Ala Val Gln Lys Leu Tyr
305 310 315 320

Glu His Ile Val Ala Asp Asp Arg Phe Thr Lys Ser Ile Ser Ile Gly
325 330 335

Pro Ile Ser Lys Thr Ile Asn Met Leu Val Arg Trp Tyr Val Asp Gly
340 345 350

Pro Ala Ser Thr Ala Phe Gln Glu His Val Ser Arg Ile Pro Asp Tyr
355 360 365

Leu Trp Met Gly Leu Asp Gly Met Lys Met Gln Gly Thr Asn Gly Ser
370 375 380

Gln Ile Trp Asp Thr Ala Phe Ala Ile Gln Ala Leu Leu Glu Ala Gly
385 390 395 400

Gly His His Arg Pro Glu Phe Ser Ser Cys Leu Gln Lys Ala His Glu
405 410 415

Phe Leu Arg Leu Ser Gln Val Pro Asp Asn Pro Pro Asp Tyr Gln Lys
420 425 430

Tyr Tyr Arg Gln Met Arg Lys Gly Gly Phe Ser Phe Ser Thr Leu Asp
435 440 445

Cys Gly Trp Ile Val Ser Asp Cys Thr Ala Glu Ala Leu Lys Ala Val
450 455 460

Leu Leu Leu Gln Glu Lys Cys Pro His Val Thr Glu His Ile Pro Arg
465 470 475 480

- 182 -

Glu Arg Leu Cys Asp Ala Val Ala Val Leu Leu Asn Met Arg Asn Pro
 485 490 495

Asp Gly Gly Phe Ala Thr Tyr Glu Thr Lys Arg Gly Gly His Leu Leu
 500 505 510

Glu Leu Leu Asn Pro Ser Glu Val Phe Gly Asp Ile Met Ile Asp Tyr
 515 520 525

Thr Tyr Val Glu Cys Thr Ser Ala Val Met Gln Ala Leu Lys Tyr Phe
 530 535 540

His Lys Arg Phe Pro Glu His Arg Ala Ala Glu Ile Arg Glu Thr Leu
 545 550 555 560

Thr Gln Gly Leu Glu Phe Cys Arg Arg Gln Gln Arg Ala Asp Gly Ser
 565 570 575

Trp Glu Gly Ser Trp Gly Val Cys Phe Thr Tyr Gly Thr Trp Phe Gly
 580 585 590

Leu Glu Ala Phe Ala Cys Met Gly Gln Thr Tyr Arg Asp Gly Thr Ala
 595 600 605

Cys Ala Glu Val Ser Arg Ala Cys Asp Phe Leu Leu Ser Arg Gln Met
 610 615 620

Ala Asp Gly Gly Trp Gly Glu Asp Phe Glu Ser Cys Glu Glu Arg Arg
 625 630 635 640

Tyr Leu Gln Ser Ala Gln Ser Gln Ile His Asn Thr Cys Trp Ala Met
 645 650 655

Met Gly Leu Met Ala Val Arg His Pro Asp Ile Glu Ala Gln Glu Arg
 660 665 670

Gly Val Arg Cys Leu Leu Glu Lys Gln Leu Pro Asn Gly Asp Trp Pro
 675 680 685

Gln Glu Asn Ile Ala Gly Val Phe Asn Lys Ser Cys Ala Ile Ser Tyr
 690 695 700

Thr Ser Tyr Arg Asn Ile Phe Pro Ile Trp Ala Leu Gly Arg Phe Ser
 705 710 715 720

- 183 -

Gln Leu Tyr Pro Glu Arg Ala Leu Ala Gly His Pro
 725 730

<210> 98

<211> 228

<212> PRT

<213> Homo sapiens

<400> 98

Met Met Pro Glu Ile Asn Thr Asn His Leu Asp Lys Gln Gln Val Gln
 1 5 10 15

Leu Leu Ala Glu Met Cys Ile Leu Ile Asp Glu Asn Asp Asn Lys Ile
 20 25 30

Gly Ala Glu Thr Lys Lys Asn Cys His Leu Asn Glu Asn Ile Glu Lys
 35 40 45

Gly Leu Leu His Arg Ala Phe Ser Val Phe Leu Phe Asn Thr Glu Asn
 50 55 60

Lys Leu Leu Leu Gln Gln Arg Ser Asp Ala Lys Ile Thr Phe Pro Gly
 65 70 75 80

Cys Phe Thr Asn Thr Cys Cys Ser His Pro Leu Ser Asn Pro Ala Glu
 85 90 95

Leu Glu Glu Ser Asp Ala Leu Gly Val Arg Arg Ala Ala Gln Arg Arg
 100 105 110

Leu Lys Ala Glu Leu Gly Ile Pro Leu Glu Glu Val Pro Pro Glu Glu
 115 120 125

Ile Asn Tyr Leu Thr Arg Ile His Tyr Lys Ala Gln Ser Asp Gly Ile
 130 135 140

Trp Gly Glu His Glu Ile Asp Tyr Ile Leu Leu Val Arg Lys Asn Val
 145 150 155 160

- 184 -

Thr Leu Asn Pro Asp Pro Asn Glu Ile Lys Ser Tyr Cys Tyr Val Ser
 165 170 175

Lys Glu Glu Leu Lys Glu Leu Leu Lys Lys Ala Ala Ser Gly Glu Ile
 180 185 190

Lys Ile Thr Pro Trp Phe Lys Ile Ile Ala Ala Thr Phe Leu Phe Lys
 195 200 205

Trp Trp Asp Asn Leu Asn His Leu Asn Gln Phe Val Asp His Glu Lys
 210 215 220

Ile Tyr Arg Met
 225

<210> 99

<211> 302

<212> PRT

<213> Homo sapiens

<400> 99

Met Ala Trp Lys Arg Leu Gly Ala Leu Val Met Phe Pro Leu Gln Met
 1 5 10 15

Ile Tyr Leu Val Val Lys Ala Ala Val Gly Leu Val Leu Pro Ala Lys
 20 25 30

Leu Arg Asp Leu Ser Arg Glu Asn Val Leu Ile Thr Gly Gly Gly Arg
 35 40 45

Gly Ile Gly Arg Gln Leu Ala Arg Glu Phe Ala Glu Arg Gly Ala Arg
 50 55 60

Lys Ile Val Leu Trp Gly Arg Thr Glu Lys Cys Leu Lys Glu Thr Thr
 65 70 75 80

Glu Glu Ile Arg Gln Met Gly Thr Glu Cys His Tyr Phe Ile Cys Asp
 85 90 95

Val Gly Asn Arg Glu Glu Val Tyr Gln Thr Ala Lys Ala Val Arg Glu
 100 105 110

- 185 -

Lys Val Gly Asp Ile Thr Ile Leu Val Asn Asn Ala Ala Val Val His
115 120 125

Gly Lys Ser Leu Met Asp Ser Asp Asp Asp Ala Leu Leu Lys Ser Gln
130 135 140

His Ile Asn Thr Leu Gly Gln Phe Trp Thr Thr Lys Ala Phe Leu Pro
145 150 155 160

Arg Met Leu Glu Leu Gln Asn Gly His Ile Val Cys Leu Asn Ser Val
165 170 175

Leu Ala Leu Ser Ala Ile Pro Gly Ala Ile Asp Tyr Cys Thr Ser Lys
180 185 190

Ala Ser Ala Phe Ala Phe Met Glu Ser Leu Thr Leu Gly Leu Leu Asp
195 200 205

Cys Pro Gly Val Ser Ala Thr Thr Val Leu Pro Phe His Thr Ser Thr
210 215 220

Glu Met Phe Gln Gly Met Arg Val Arg Phe Pro Asn Leu Phe Pro Pro
225 230 235 240

Leu Lys Pro Glu Thr Val Ala Arg Arg Thr Val Glu Ala Val Gln Leu
245 250 255

Asn Gln Ala Leu Leu Leu Leu Pro Trp Thr Met His Ala Leu Val Ile
260 265 270

Leu Lys Ser Ile Leu Pro Gln Ala Ala Leu Glu Glu Ile His Lys Phe
275 280 285

Ser Gly Thr Tyr Thr Cys Met Asn Thr Phe Lys Gly Arg Thr
290 295 300

<210> 100

<211> 674

<212> PRT

<213> Homo sapiens

- 186 -

<400> 100

Met	Pro	Ser	Tyr	Thr	Val	Thr	Val	Ala	Thr	Gly	Ser	Gln	Trp	Phe	Ala
1				5					10					15	
Gly	Thr	Asp	Asp	Tyr	Ile	Tyr	Leu	Ser	Leu	Val	Gly	Ser	Ala	Gly	Cys
		20						25					30		
Ser	Glu	Lys	His	Leu	Leu	Asp	Lys	Pro	Phe	Tyr	Asn	Asp	Phe	Glu	Arg
		35					40					45			
Gly	Ala	Val	Asp	Ser	Tyr	Asp	Val	Thr	Val	Asp	Glu	Glu	Leu	Gly	Glu
	50					55					60				
Ile	Gln	Leu	Val	Arg	Ile	Glu	Lys	Arg	Lys	Tyr	Trp	Leu	Asn	Asp	Asp
65					70					75				80	
Trp	Tyr	Leu	Lys	Tyr	Ile	Thr	Leu	Lys	Thr	Pro	His	Gly	Asp	Tyr	Ile
				85					90					95	
Glu	Phe	Pro	Cys	Tyr	Arg	Trp	Ile	Thr	Gly	Asp	Val	Glu	Val	Val	Leu
			100					105					110		
Arg	Asp	Gly	Arg	Ala	Lys	Leu	Ala	Arg	Asp	Asp	Gln	Ile	His	Ile	Leu
		115					120					125			
Lys	Gln	His	Arg	Arg	Lys	Glu	Leu	Glu	Thr	Arg	Gln	Lys	Gln	Tyr	Arg
	130					135					140				
Trp	Met	Glu	Trp	Asn	Pro	Gly	Phe	Pro	Leu	Ser	Ile	Asp	Ala	Lys	Cys
145					150					155					160
His	Lys	Asp	Leu	Pro	Arg	Asp	Ile	Gln	Phe	Asp	Ser	Glu	Lys	Gly	Val
				165				170						175	
Asp	Phe	Val	Leu	Asn	Tyr	Ser	Lys	Ala	Met	Glu	Asn	Leu	Phe	Ile	Asn
			180					185					190		
Arg	Phe	Met	His	Met	Phe	Gln	Ser	Ser	Trp	Asn	Asp	Phe	Ala	Asp	Phe
		195					200					205			
Glu	Lys	Ile	Phe	Val	Lys	Ile	Ser	Asn	Thr	Ile	Ser	Glu	Arg	Val	Met
	210					215					220				

- 187 -

Asn His Trp Gln Glu Asp Leu Met Phe Gly Tyr Gln Phe Leu Asn Gly
 225 230 235 240

Cys Asn Pro Val Leu Ile Arg Arg Cys Thr Glu Leu Pro Glu Lys Leu
 245 250 255

Pro Val Thr Thr Glu Met Val Glu Cys Ser Leu Glu Arg Gln Leu Ser
 260 265 270

Leu Glu Gln Glu Val Gln Gln Gly Asn Ile Phe Ile Val Asp Phe Glu
 275 280 285

Leu Leu Asp Gly Ile Asp Ala Asn Lys Thr Asp Pro Cys Thr Leu Gln
 290 295 300

Phe Leu Ala Ala Pro Ile Cys Leu Leu Tyr Lys Asn Leu Ala Asn Lys
 305 310 315 320

Ile Val Pro Ile Ala Ile Gln Leu Asn Gln Ile Pro Gly Asp Glu Asn
 325 330 335

Pro Ile Phe Leu Pro Ser Asp Ala Lys Tyr Asp Trp Leu Leu Ala Lys
 340 345 350

Ile Trp Val Arg Ser Ser Asp Phe His Val His Gln Thr Ile Thr His
 355 360 365

Leu Leu Arg Thr His Leu Val Ser Glu Val Phe Gly Ile Ala Met Tyr
 370 375 380

Arg Gln Leu Pro Ala Val His Pro Ile Phe Lys Leu Leu Val Ala His
 385 390 395 400

Val Arg Phe Thr Ile Ala Ile Asn Thr Lys Ala Arg Glu Gln Leu Ile
 405 410 415

Cys Glu Cys Gly Leu Phe Asp Lys Ala Asn Ala Thr Gly Gly Gly Gly
 420 425 430

His Val Gln Met Val Gln Arg Ala Met Lys Asp Leu Thr Tyr Ala Ser
 435 440 445

Leu Cys Phe Pro Glu Ala Ile Lys Ala Arg Gly Met Glu Ser Lys Glu
 450 455 460

- 188 -

Asp Ile Pro Tyr Tyr Phe Tyr Arg Asp Asp Gly Leu Leu Val Trp Glu
465 470 475 480

Ala Ile Arg Thr Phe Thr Ala Glu Val Val Asp Ile Tyr Tyr Glu Gly
485 490 495

Asp Gln Val Val Glu Glu Asp Pro Glu Leu Gln Asp Phe Val Asn Asp
500 505 510

Val Tyr Val Tyr Gly Met Arg Gly Arg Lys Ser Ser Gly Phe Pro Lys
515 520 525

Ser Val Lys Ser Arg Glu Gln Leu Ser Glu Tyr Leu Thr Val Val Ile
530 535 540

Phe Thr Ala Ser Ala Gln His Ala Ala Val Asn Phe Gly Gln Tyr Asp
545 550 555 560

Trp Cys Ser Trp Ile Pro Asn Ala Pro Pro Thr Met Arg Ala Pro Pro
565 570 575

Pro Thr Ala Lys Gly Val Val Thr Ile Glu Gln Ile Val Asp Thr Leu
580 585 590

Pro Asp Arg Gly Arg Ser Cys Trp His Leu Gly Ala Val Trp Ala Leu
595 600 605

Ser Gln Phe Gln Glu Asn Glu Leu Phe Leu Gly Met Tyr Pro Glu Glu
610 615 620

His Phe Ile Glu Lys Pro Val Lys Glu Ala Met Ala Arg Phe Arg Lys
625 630 635 640

Asn Leu Glu Ala Ile Val Ser Val Ile Ala Glu Arg Asn Lys Lys Lys
645 650 655

Gln Leu Pro Tyr Tyr Tyr Leu Ser Pro Asp Arg Ile Pro Asn Ser Val
660 665 670

Ala Ile

- 189 -

<210> 101

<211> 299

<212> PRT

<213> Homo sapiens

<400> 101

Met Asp Leu Val Leu Arg Val Ala Asp Tyr Tyr Phe Phe Thr Pro Tyr
 1 5 10 15

Val Tyr Pro Ala Thr Trp Pro Glu Asp Asp Ile Phe Arg Gln Ala Ile
 20 25 30

Ser Leu Leu Ile Val Thr Asn Val Gly Ala Tyr Ile Leu Tyr Phe Phe
 35 40 45

Cys Ala Thr Leu Ser Tyr Tyr Phe Val Phe Asp His Ala Leu Met Lys
 50 55 60

His Pro Gln Phe Leu Lys Asn Gln Val Arg Arg Glu Ile Lys Phe Thr
 65 70 75 80

Val Gln Ala Leu Pro Trp Ile Ser Ile Leu Thr Val Ala Leu Phe Leu
 85 90 95

Leu Glu Ile Arg Gly Tyr Ser Lys Leu His Asp Asp Leu Gly Glu Phe
 100 105 110

Pro Tyr Gly Leu Phe Glu Leu Val Val Ser Ile Ile Ser Phe Leu Phe
 115 120 125

Phe Thr Asp Met Phe Ile Tyr Trp Ile His Arg Gly Leu His His Arg
 130 135 140

Leu Val Tyr Lys Arg Leu His Lys Pro His His Ile Trp Lys Ile Pro
 145 150 155 160

Thr Pro Phe Ala Ser His Ala Phe His Pro Ile Asp Gly Phe Leu Gln
 165 170 175

Ser Leu Pro Tyr His Ile Tyr Pro Phe Ile Phe Pro Leu His Lys Val
 180 185 190

- 190 -

Val Tyr Leu Ser Leu Tyr Ile Leu Val Asn Ile Trp Thr Ile Ser Ile
195 200 205

His Asp Gly Asp Phe Arg Val Pro Gln Ile Leu Gln Pro Phe Ile Asn
210 215 220

Gly Ser Ala His His Thr Asp His His Met Phe Phe Asp Tyr Asn Tyr
225 230 235 240

Gly Gln Tyr Phe Thr Leu Trp Asp Arg Ile Gly Gly Ser Phe Lys Asn
245 250 255

Pro Ser Ser Phe Glu Gly Lys Gly Pro Leu Ser Tyr Val Lys Glu Met
260 265 270

Thr Glu Gly Lys Arg Ser Ser Pro Ser Gly Asn Gly Cys Lys Asn Glu
275 280 285

Lys Leu Phe Asn Gly Glu Phe Thr Lys Thr Glu
290 295

<210> 102

<211> 676

<212> PRT

<213> Homo sapiens

<400> 102

Met Ala Glu Phe Arg Val Arg Val Ser Thr Gly Glu Ala Phe Gly Ala
1 5 10 15

Gly Thr Trp Asp Lys Val Ser Val Ser Ile Val Gly Thr Arg Gly Glu
20 25 30

Ser Pro Pro Leu Pro Leu Asp Asn Leu Gly Lys Glu Phe Thr Ala Gly
35 40 45

Ala Glu Glu Asp Phe Gln Val Thr Leu Pro Glu Asp Val Gly Arg Val
50 55 60

Leu Leu Leu Arg Val His Lys Ala Pro Pro Val Leu Pro Leu Leu Gly
65 70 75 80

- 191 -

Pro Leu Ala Pro Asp Ala Trp Phe Cys Arg Trp Phe Gln Leu Thr Pro
 85 90 95

Pro Arg Gly Gly His Leu Leu Phe Pro Cys Tyr Gln Trp Leu Glu Gly
 100 105 110

Ala Gly Thr Leu Val Leu Gln Glu Gly Thr Ala Lys Val Ser Trp Ala
 115 120 125

Asp His His Pro Val Leu Gln Gln Gln Arg Gln Glu Glu Leu Gln Ala
 130 135 140

Arg Gln Glu Met Tyr Gln Trp Lys Ala Tyr Asn Pro Gly Trp Pro His
 145 150 155 160

Cys Leu Asp Glu Lys Thr Val Glu Asp Leu Glu Leu Asn Ile Lys Tyr
 165 170 175

Ser Thr Ala Lys Asn Ala Asn Phe Tyr Leu Gln Ala Gly Ser Ala Phe
 180 185 190

Ala Glu Met Lys Ile Lys Gly Leu Leu Asp Arg Lys Gly Leu Trp Arg
 195 200 205

Ser Leu Asn Glu Met Lys Arg Ile Phe Asn Phe Arg Arg Thr Pro Ala
 210 215 220

Ala Glu His Ala Phe Glu His Trp Gln Glu Asp Ala Phe Phe Ala Ser
 225 230 235 240

Gln Phe Leu Asn Gly Leu Asn Pro Val Leu Ile Arg Arg Cys His Tyr
 245 250 255

Leu Pro Lys Asn Phe Pro Val Thr Asp Ala Met Val Ala Ser Leu Leu
 260 265 270

Gly Pro Gly Thr Ser Leu Gln Ala Glu Leu Glu Lys Gly Ser Leu Phe
 275 280 285

Leu Val Asp His Gly Ile Leu Ser Gly Ile Gln Thr Asn Val Ile Asn
 290 295 300

- 192 -

Gly Lys Pro Gln Phe Ser Ala Ala Pro Met Thr Leu Leu Tyr Gln Ser
305 310 315 320

Pro Gly Cys Gly Pro Leu Leu Pro Leu Ala Ile Gln Leu Ser Gln Thr
325 330 335

Pro Gly Pro Asn Ser Pro Ile Phe Leu Pro Thr Asp Asp Lys Trp Asp
340 345 350

Trp Leu Leu Ala Lys Thr Trp Val Arg Asn Ala Glu Phe Ser Phe His
355 360 365

Glu Ala Leu Thr His Leu Leu His Ser His Leu Leu Pro Glu Val Phe
370 375 380

Thr Leu Ala Thr Leu Arg Gln Leu Pro His Cys His Pro Leu Phe Lys
385 390 395 400

Leu Leu Ile Pro His Thr Arg Tyr Thr Leu His Ile Asn Thr Leu Ala
405 410 415

Arg Glu Leu Leu Ile Val Pro Gly Gln Val Val Asp Arg Ser Thr Gly
420 425 430

Ile Gly Ile Glu Gly Phe Ser Glu Leu Ile Gln Arg Asn Met Lys Gln
435 440 445

Leu Asn Tyr Ser Leu Leu Cys Leu Pro Glu Asp Ile Arg Thr Arg Gly
450 455 460

Val Glu Asp Ile Pro Gly Tyr Tyr Tyr Arg Asp Asp Gly Met Gln Ile
465 470 475 480

Trp Gly Ala Val Glu Arg Phe Val Ser Glu Ile Ile Gly Ile Tyr Tyr
485 490 495

Pro Ser Asp Glu Ser Val Gln Asp Asp Arg Glu Leu Gln Ala Trp Val
500 505 510

Arg Glu Ile Phe Ser Lys Gly Phe Leu Asn Gln Glu Ser Ser Gly Ile
515 520 525

Pro Ser Ser Leu Glu Thr Arg Glu Ala Leu Val Gln Tyr Val Thr Met
530 535 540

- 193 -

Val Ile Phe Thr Cys Ser Ala Lys His Ala Ala Val Ser Ala Gly Gln
545 550 555 560

Phe Asp Ser Cys Ala Trp Met Pro Asn Leu Pro Pro Ser Met Gln Leu
565 570 575

Pro Pro Pro Thr Ser Lys Gly Leu Ala Thr Cys Glu Gly Phe Ile Ala
580 585 590

Thr Leu Pro Pro Val Asn Ala Thr Cys Asp Val Ile Leu Ala Leu Trp
595 600 605

Leu Leu Ser Lys Glu Pro Gly Asp Gln Arg Pro Leu Gly Thr Tyr Pro
610 615 620

Asp Glu His Phe Thr Glu Glu Ala Pro Arg Arg Ser Ile Ala Thr Phe
625 630 635 640

Gln Ser Arg Leu Ala Gln Ile Ser Arg Gly Ile Gln Glu Arg Asn Arg
645 650 655

Gly Leu Val Leu Pro Tyr Thr Tyr Leu Asp Pro Pro Leu Ile Glu Asn
660 665 670

Ser Val Ser Ile
675

<210> 103

<211> 311

<212> PRT

<213> Homo sapiens

<400> 103

Arg Thr Arg Gly Ala His Ile Ile Ala Leu Glu Ser Ile Ala Trp Phe
1 5 10 15

Thr Val Phe Tyr Phe Gly Asn Gly Trp Ile Pro Thr Leu Ile Thr Ala
20 25 30

Phe Val Leu Ala Thr Ser Gln Ala Gln Ala Gly Trp Leu Gln His Asp
35 40 45

- 194 -

Tyr Gly His Leu Ser Val Tyr Arg Lys Pro Lys Trp Asn His Leu Val
50 55 60

His Lys Phe Val Ile Gly His Leu Lys Gly Ala Ser Ala Asn Trp Trp
65 70 75 80

Asn His Arg His Phe Gln His His Ala Lys Pro Asn Ile Phe His Lys
85 90 95

Asp Pro Asp Val Asn Met Leu His Val Phe Val Leu Gly Glu Trp Gln
100 105 110

Pro Ile Glu Tyr Gly Lys Lys Lys Leu Lys Tyr Leu Pro Tyr Asn His
115 120 125

Gln His Glu Tyr Phe Phe Leu Ile Gly Pro Pro Leu Leu Ile Pro Met
130 135 140

Tyr Phe Gln Tyr Gln Ile Ile Met Thr Met Ile Val His Lys Asn Trp
145 150 155 160

Val Asp Leu Ala Trp Ala Val Ser Tyr Tyr Ile Arg Phe Phe Ile Thr
165 170 175

Tyr Ile Pro Phe Tyr Gly Ile Leu Gly Ala Leu Leu Phe Leu Asn Phe
180 185 190

Ile Arg Phe Leu Glu Ser His Trp Phe Val Trp Val Thr Gln Met Asn
195 200 205

His Ile Val Met Glu Ile Asp Gln Glu Ala Tyr Arg Asp Trp Phe Ser
210 215 220

Ser Gln Leu Thr Ala Thr Cys Asn Val Glu Gln Ser Phe Phe Asn Asp
225 230 235 240

Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu His His Leu Phe Pro
245 250 255

Thr Met Pro Arg His Asn Leu His Lys Ile Ala Pro Leu Val Lys Ser
260 265 270

- 195 -

Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Glu Lys Pro Leu Leu Arg
275 280 285

Ala Leu Leu Asp Ile Ile Arg Asp Leu Met Lys Ser Gly Lys Leu Trp
290 295 300

Leu Asp Ala Tyr Leu His Lys
305 310

<210> 104

<211> 475

<212> PRT

<213> Homo sapiens

<400> 104

Met Ala Ala Lys Leu Gln Pro Asn Ile Pro Lys Ala Lys Ser Leu Asp
1 5 10 15

Gly Val Thr Asn Asp Arg Thr Ala Ser Gln Gly Gln Trp Gly Arg Ala
20 25 30

Trp Glu Val Asp Trp Phe Ser Leu Ala Ser Val Ile Phe Leu Leu Leu
35 40 45

Phe Ala Pro Phe Ile Val Tyr Tyr Phe Ile Met Ala Cys Asp Gln Tyr
50 55 60

Ser Cys Ala Leu Thr Gly Pro Val Val Asp Ile Val Thr Gly His Ala
65 70 75 80

Arg Leu Ser Asp Ile Trp Ala Lys Thr Pro Pro Ile Thr Arg Lys Ala
85 90 95

Ala Gln Leu Tyr Thr Leu Trp Val Thr Phe Gln Val Leu Leu Tyr Thr
100 105 110

Ser Leu Pro Asp Phe Cys His Lys Phe Leu Pro Gly Tyr Val Gly Gly
115 120 125

Ile Gln Glu Gly Ala Val Thr Pro Ala Gly Val Val Asn Lys Tyr Gln
130 135 140

- 196 -

Ile Asn Gly Leu Gln Ala Trp Leu Leu Thr His Leu Leu Trp Phe Ala
 145 150 155 160

Asn Ala His Leu Leu Ser Trp Phe Ser Pro Thr Ile Ile Phe Asp Asn
 165 170 175

Trp Ile Pro Leu Leu Trp Cys Ala Asn Ile Leu Gly Tyr Ala Val Ser
 180 185 190

Thr Phe Ala Met Val Lys Gly Tyr Phe Phe Pro Thr Ser Ala Arg Asp
 195 200 205

Cys Lys Phe Thr Gly Asn Phe Phe Tyr Asn Tyr Met Met Gly Ile Glu
 210 215 220

Phe Asn Pro Arg Ile Gly Lys Trp Phe Asp Phe Lys Leu Phe Phe Asn
 225 230 235 240

Gly Arg Pro Gly Ile Val Ala Trp Thr Leu Ile Asn Leu Ser Phe Ala
 245 250 255

Ala Lys Gln Arg Glu Leu His Ser His Val Thr Asn Ala Met Val Leu
 260 265 270

Val Asn Val Leu Gln Ala Ile Tyr Val Ile Asp Phe Phe Trp Asn Glu
 275 280 285

Thr Trp Tyr Leu Lys Thr Ile Asp Ile Cys His Asp His Phe Gly Trp
 290 295 300

Tyr Leu Gly Trp Gly Asp Cys Val Trp Leu Pro Tyr Leu Tyr Thr Leu
 305 310 315 320

Gln Gly Leu Tyr Leu Val Tyr His Pro Val Gln Leu Ser Thr Pro His
 325 330 335

Ala Val Gly Val Leu Leu Leu Gly Leu Val Gly Tyr Tyr Ile Phe Arg
 340 345 350

Val Ala Asn His Gln Lys Asp Leu Phe Arg Arg Thr Asp Gly Arg Cys
 355 360 365

Leu Ile Trp Gly Arg Lys Pro Lys Val Ile Glu Cys Ser Tyr Thr Ser
 370 375 380

- 197 -

Ala Asp Gly Gln Arg His His Ser Lys Leu Leu Val Ser Gly Phe Trp
385 390 395 400

Gly Val Ala Arg His Phe Asn Tyr Val Gly Asp Leu Met Gly Ser Leu
405 410 415

Ala Tyr Cys Leu Ala Cys Gly Gly Gly His Leu Leu Pro Tyr Phe Tyr
420 425 430

Ile Ile Tyr Met Ala Ile Leu Leu Thr His Arg Cys Leu Arg Asp Glu
435 440 445

His Arg Cys Ala Ser Lys Tyr Gly Arg Asp Trp Glu Arg Tyr Thr Ala
450 455 460

Ala Val Pro Tyr Arg Leu Leu Pro Gly Ile Phe
465 470 475

<210> 105

<211> 359

<212> PRT

<213> Homo sapiens

<400> 105

Met Pro Ala His Leu Leu Gln Asp Asp Ile Ser Ser Ser Tyr Thr Thr
1 5 10 15

Thr Thr Thr Ile Thr Ala Pro Pro Pro Gly Val Leu Gln Asn Gly Gly
20 25 30

Asp Lys Leu Glu Thr Met Pro Leu Tyr Leu Glu Asp Asp Ile Arg Pro
35 40 45

Asp Ile Lys Asp Asp Ile Tyr Asp Pro Thr Tyr Lys Asp Lys Glu Gly
50 55 60

Pro Ser Pro Lys Val Glu Tyr Val Trp Arg Asn Ile Ile Leu Met Ser
65 70 75 80

- 198 -

Leu Leu His Leu Gly Ala Leu Tyr Gly Ile Thr Leu Ile Pro Thr Cys
85 90 95

Lys Phe Tyr Thr Trp Leu Trp Gly Val Phe Tyr Tyr Phe Val Ser Ala
100 105 110

Leu Gly Ile Thr Ala Gly Ala His Arg Leu Trp Ser His Arg Ser Tyr
115 120 125

Lys Ala Arg Leu Pro Leu Arg Leu Phe Leu Ile Ile Ala Asn Thr Met
130 135 140

Ala Phe Gln Asn Asp Val Tyr Glu Trp Ala Arg Asp His Arg Ala His
145 150 155 160

His Lys Phe Ser Glu Thr His Ala Asp Pro His Asn Ser Arg Arg Gly
165 170 175

Phe Phe Phe Ser His Val Gly Trp Leu Leu Val Arg Lys His Pro Ala
180 185 190

Val Lys Glu Lys Gly Ser Thr Leu Asp Leu Ser Asp Leu Glu Ala Glu
195 200 205

Lys Leu Val Met Phe Gln Arg Arg Tyr Tyr Lys Pro Gly Leu Leu Met
210 215 220

Met Cys Phe Ile Leu Pro Thr Leu Val Pro Trp Tyr Phe Trp Gly Glu
225 230 235 240

Thr Phe Gln Asn Ser Val Phe Val Ala Thr Phe Leu Arg Tyr Ala Val
245 250 255

Val Leu Asn Ala Thr Trp Leu Val Asn Ser Ala Ala His Leu Phe Gly
260 265 270

Tyr Arg Pro Tyr Asp Lys Asn Ile Ser Pro Arg Glu Asn Ile Leu Val
275 280 285

Ser Leu Gly Ala Val Gly Glu Gly Phe His Asn Tyr His His Ser Phe
290 295 300

Pro Tyr Asp Tyr Ser Ala Ser Glu Tyr Arg Trp His Ile Asn Phe Asn
305 310 315 320

- 199 -

Thr Phe Phe Ile Asp Trp Met Ala Ala Leu Gly Leu Thr Tyr Asp Arg
 325 330 335

Lys Lys Val Ser Lys Ala Ala Ile Leu Ala Arg Ile Lys Arg Thr Gly
 340 345 350

Asp Gly Asn Tyr Lys Ser Gly
 355

<210> 106

<211> 339

<212> PRT

<213> Homo sapiens

<400> 106

Met Ala Val Ala Gln Gln Leu Arg Ala Glu Ser Asp Phe Glu Gln Leu
 1 5 10 15

Pro Asp Asp Val Ala Ile Ser Ala Asn Ile Ala Asp Ile Glu Glu Lys
 20 25 30

Arg Gly Phe Thr Ser His Phe Val Phe Val Ile Glu Val Lys Thr Lys
 35 40 45

Gly Gly Ser Lys Tyr Leu Ile Tyr Arg Arg Tyr Arg Gln Phe His Ala
 50 55 60

Leu Gln Ser Lys Leu Glu Glu Arg Phe Gly Pro Asp Ser Lys Ser Ser
 65 70 75 80

Ala Leu Ala Cys Thr Leu Pro Thr Leu Pro Ala Lys Val Tyr Val Gly
 85 90 95

Val Lys Gln Glu Ile Ala Glu Met Arg Ile Pro Ala Leu Asn Ala Tyr
 100 105 110

Met Lys Ser Leu Leu Ser Leu Pro Val Trp Val Leu Met Asp Glu Asp
 115 120 125

Val Arg Ile Phe Phe Tyr Gln Ser Pro Tyr Asp Ser Glu Gln Val Pro
 130 135 140

- 200 -

Gln Ala Ile Arg Arg Leu Arg Pro Arg Thr Arg Lys Val Lys Ser Val
145 150 155 160

Ser Pro Gln Gly Asn Ser Val Asp Arg Met Ala Ala Pro Arg Ala Glu
165 170 175

Ala Leu Phe Asp Phe Thr Gly Asn Ser Lys Leu Glu Leu Asn Phe Lys
180 185 190

Ala Gly Asp Val Ile Phe Leu Leu Ser Arg Ile Asn Lys Asp Trp Leu
195 200 205

Glu Gly Thr Val Arg Gly Ala Thr Gly Ile Phe Pro Leu Ser Phe Val
210 215 220

Lys Ile Leu Lys Asp Phe Pro Glu Glu Asp Asp Pro Thr Asn Trp Leu
225 230 235 240

Arg Cys Tyr Tyr Tyr Glu Asp Thr Ile Ser Thr Ile Lys Asp Ile Ala
245 250 255

Val Glu Glu Asp Leu Ser Ser Thr Pro Leu Leu Lys Asp Leu Leu Glu
260 265 270

Leu Thr Arg Arg Glu Phe Gln Arg Glu Asp Ile Ala Leu Asn Tyr Arg
275 280 285

Asp Ala Glu Gly Asp Leu Val Arg Leu Leu Ser Asp Glu Asp Val Ala
290 295 300

Leu Met Val Arg Gln Ala Arg Gly Leu Pro Ser Gln Lys Arg Leu Phe
305 310 315 320

Pro Trp Lys Leu His Ile Thr Gln Lys Asp Asn Tyr Arg Val Tyr Asn
325 330 335

- 201 -

Thr Met Pro

<210> 107

<211> 323

<212> PRT

<213> Homo sapiens

<400> 107

Met Asp Ser Lys Gln Gln Cys Val Lys Leu Asn Asp Gly His Phe Met
1 5 10 15

Pro Val Leu Gly Phe Gly Thr Tyr Ala Pro Pro Glu Val Pro Arg Ser
20 25 30

Lys Ala Leu Glu Val Thr Lys Leu Ala Ile Glu Ala Gly Phe Arg His
35 40 45

Ile Asp Ser Ala His Leu Tyr Asn Asn Glu Glu Gln Val Gly Leu Ala
50 55 60

Ile Arg Ser Lys Ile Ala Asp Gly Ser Val Lys Arg Glu Asp Ile Phe
65 70 75 80

Tyr Thr Ser Lys Leu Trp Ser Thr Phe His Arg Pro Glu Leu Val Arg
85 90 95

Pro Ala Leu Glu Asn Ser Leu Lys Lys Ala Gln Leu Asp Tyr Val Asp
100 105 110

Leu Tyr Leu Ile His Ser Pro Met Ser Leu Lys Pro Gly Glu Glu Leu
115 120 125

Ser Pro Thr Asp Glu Asn Gly Lys Val Ile Phe Asp Ile Val Asp Leu
130 135 140

Cys Thr Thr Trp Glu Ala Met Glu Lys Cys Lys Asp Ala Gly Leu Ala
145 150 155 160

Lys Ser Ile Gly Val Ser Asn Phe Asn Arg Arg Gln Leu Glu Met Ile
165 170 175

- 202 -

Leu Asn Lys Pro Gly Leu Lys Tyr Lys Pro Val Cys Asn Gln Val Glu
 180 185 190

Cys His Pro Tyr Phe Asn Arg Ser Lys Leu Leu Asp Phe Cys Lys Ser
 195 200 205

Lys Asp Ile Val Leu Val Ala Tyr Ser Ala Leu Gly Ser Gln Arg Asp
 210 215 220

Lys Arg Trp Val Asp Pro Asn Ser Pro Val Leu Leu Glu Asp Pro Val
 225 230 235 240

Leu Cys Ala Leu Ala Lys Lys His Lys Arg Thr Pro Ala Leu Ile Ala
 245 250 255

Leu Arg Tyr Gln Leu Gln Arg Gly Val Val Val Leu Ala Lys Ser Tyr
 260 265 270

Asn Glu Gln Arg Ile Arg Gln Asn Val Gln Val Phe Glu Phe Gln Leu
 275 280 285

Thr Ala Glu Asp Met Lys Ala Ile Asp Gly Leu Asp Arg Asn Leu His
 290 295 300

Tyr Phe Asn Ser Asp Ser Phe Ala Ser His Pro Asn Tyr Pro Tyr Ser
 305 310 315 320

Asp Glu Tyr

<210> 108

<211> 588

<212> PRT

<213> Homo sapiens

<400> 108

Met Gly Gly Thr Ala Arg Gly Pro Gly Arg Lys Asp Ala Gly Pro Pro
 1 5 10 15

Gly Ala Gly Leu Pro Pro Gln Gln Arg Arg Leu Gly Asp Gly Val Tyr
 20 25 30

- 203 -

Asp Thr Phe Met Met Ile Asp Glu Thr Lys Cys Pro Pro Cys Ser Asn
 35 40 45

Val Leu Cys Asn Pro Ser Glu Pro Pro Pro Pro Arg Arg Leu Asn Met
 50 55 60

Thr Thr Glu Gln Phe Thr Gly Asp His Thr Gln His Phe Leu Asp Gly
 65 70 75 80

Gly Glu Met Lys Val Glu Gln Leu Phe Gln Glu Phe Gly Asn Arg Lys
 85 90 95

Ser Asn Thr Ile Gln Ser Asp Gly Ile Ser Asp Ser Glu Lys Cys Ser
 100 105 110

Pro Thr Val Ser Gln Gly Lys Ser Ser Asp Cys Leu Asn Thr Val Lys
 115 120 125

Ser Asn Ser Ser Ser Lys Ala Pro Lys Val Val Pro Leu Thr Pro Glu
 130 135 140

Gln Ala Leu Lys Gln Tyr Lys His His Leu Thr Ala Tyr Glu Lys Leu
 145 150 155 160

Glu Ile Ile Asn Tyr Pro Glu Ile Tyr Phe Val Gly Pro Asn Ala Lys
 165 170 175

Lys Arg His Gly Val Ile Gly Gly Pro Asn Asn Gly Gly Tyr Asp Asp
 180 185 190

Ala Asp Gly Ala Tyr Ile His Val Pro Arg Asp His Leu Ala Tyr Arg
 195 200 205

Tyr Glu Val Leu Lys Ile Ile Gly Lys Gly Ser Phe Gly Gln Val Ala
 210 215 220

Arg Val Tyr Asp His Lys Leu Arg Gln Tyr Val Ala Leu Lys Met Val
 225 230 235 240

Arg Asn Glu Lys Arg Phe His Arg Gln Ala Ala Glu Glu Ile Arg Ile
 245 250 255

Leu Glu His Leu Lys Lys Gln Asp Lys Thr Gly Ser Met Asn Val Ile

- 204 -

260					265					270					
His	Met	Leu	Glu	Ser	Phe	Thr	Phe	Arg	Asn	His	Val	Cys	Met	Ala	Phe
		275					280					285			
Glu	Leu	Leu	Ser	Ile	Asp	Leu	Tyr	Glu	Leu	Ile	Lys	Lys	Asn	Lys	Phe
	290					295					300				
Gln	Gly	Phe	Ser	Val	Gln	Leu	Val	Arg	Lys	Phe	Ala	Gln	Ser	Ile	Leu
305					310					315					320
Gln	Ser	Leu	Asp	Ala	Leu	His	Lys	Asn	Lys	Ile	Ile	His	Cys	Asp	Leu
				325					330					335	
Lys	Pro	Glu	Asn	Ile	Leu	Leu	Lys	His	His	Gly	Arg	Ser	Ser	Thr	Lys
			340					345					350		
Val	Ile	Asp	Phe	Gly	Ser	Ser	Cys	Phe	Glu	Tyr	Gln	Lys	Leu	Tyr	Thr
		355					360					365			
Tyr	Ile	Gln	Ser	Arg	Phe	Tyr	Arg	Ala	Pro	Glu	Ile	Ile	Leu	Gly	Ser
	370					375					380				
Arg	Tyr	Ser	Thr	Pro	Ile	Asp	Ile	Trp	Ser	Phe	Arg	Cys	Ile	Leu	Ala
385					390					395					400
Glu	Leu	Leu	Thr	Gly	Gln	Pro	Leu	Phe	Pro	Gly	Glu	Asp	Glu	Gly	Asp
				405					410					415	
Gln	Leu	Ala	Cys	Met	Met	Glu	Leu	Leu	Gly	Met	Pro	Pro	Pro	Lys	Leu
			420					425					430		
Leu	Glu	Gln	Ser	Lys	Arg	Ala	Lys	Tyr	Phe	Ile	Asn	Ser	Lys	Gly	Ile
		435					440					445			
Pro	Arg	Tyr	Cys	Ser	Val	Thr	Thr	Gln	Ala	Asp	Gly	Arg	Val	Val	Leu
	450					455					460				
Val	Gly	Gly	Arg	Ser	Arg	Arg	Gly	Lys	Lys	Arg	Gly	Pro	Pro	Gly	Ser
465					470					475					480
Lys	Asp	Trp	Gly	Thr	Ala	Leu	Lys	Gly	Cys	Asp	Asp	Tyr	Leu	Phe	Ile
				485					490					495	

- 205 -

Glu Phe Leu Lys Arg Cys Leu His Trp Asp Pro Ser Ala Arg Leu Thr
 500 505 510

Pro Ala Gln Ala Leu Arg His Pro Trp Ile Ser Lys Ser Val Pro Arg
 515 520 525

Pro Leu Thr Thr Ile Asp Lys Val Ser Gly Lys Arg Val Val Asn Pro
 530 535 540

Ala Ser Ala Phe Gln Gly Leu Gly Ser Lys Leu Pro Pro Val Val Gly
 545 550 555 560

Ile Ala Asn Lys Leu Lys Ala Asn Leu Met Ser Glu Thr Asn Gly Ser
 565 570 575

Ile Pro Leu Cys Ser Val Leu Pro Lys Leu Ile Ser
 580 585

<210> 109

<211> 365

<212> PRT

<213> Homo sapiens

<400> 109

Met Ser Leu Ile Arg Lys Lys Gly Phe Tyr Lys Gln Glu Leu Asn Lys
 1 5 10 15

Thr Ala Trp Glu Leu Pro Lys Thr Tyr Val Ser Pro Thr His Val Gly
 20 25 30

Ser Gly Ala Tyr Gly Ser Trp Cys Ser Ala Ile Asp Lys Arg Ser Gly
 35 40 45

Glu Lys Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Ser Glu Ile
 50 55 60

Phe Ala Lys Arg Ala Tyr Arg Glu Leu Leu Leu Lys His Met Gln
 65 70 75 80

His Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Ser Ser
 85 90 95

- 206 -

Leu Arg Asn Phe Tyr Asp Phe Tyr Leu Val Met Pro Phe Met Gln Thr
 100 105 110

Asp Leu Gln Lys Ile Met Gly Met Glu Phe Ser Glu Glu Lys Ile Gln
 115 120 125

Tyr Leu Val Tyr Gln Met Leu Lys Gly Leu Lys Tyr Ile His Ser Ala
 130 135 140

Gly Val Val His Arg Asp Leu Lys Pro Gly Asn Leu Ala Val Asn Glu
 145 150 155 160

Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Ala Asp
 165 170 175

Ala Glu Met Thr Gly Tyr Val Val Thr Arg Trp Tyr Arg Ala Pro Glu
 180 185 190

Val Ile Leu Ser Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
 195 200 205

Val Gly Cys Ile Met Ala Glu Met Leu Thr Gly Lys Thr Leu Phe Lys
 210 215 220

Gly Lys Asp Tyr Leu Asp Gln Leu Thr Gln Ile Leu Lys Val Thr Gly
 225 230 235 240

Val Pro Gly Thr Glu Phe Val Gln Lys Leu Asn Asp Lys Ala Ala Lys
 245 250 255

Ser Tyr Ile Gln Ser Leu Pro Gln Thr Pro Arg Lys Asp Phe Thr Gln
 260 265 270

Leu Phe Pro Arg Ala Ser Pro Gln Ala Ala Asp Leu Leu Glu Lys Met
 275 280 285

Leu Glu Leu Asp Val Asp Lys Arg Leu Thr Ala Ala Gln Ala Leu Thr
 290 295 300

His Pro Phe Phe Glu Pro Phe Arg Asp Pro Glu Glu Glu Thr Glu Ala
 305 310 315 320

Gln Gln Pro Phe Asp Asp Ser Leu Glu His Glu Lys Leu Thr Val Asp
 325 330 335

- 207 -

Glu Trp Lys Gln His Ile Tyr Lys Glu Ile Val Asn Phe Ser Pro Ile
 340 345 350

Ala Arg Lys Asp Ser Arg Arg Arg Ser Gly Met Lys Leu
 355 360 365

<210> 110

<211> 379

<212> PRT

<213> Homo sapiens

<400> 110

Met Ala Ala Ala Ala Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg
 1 5 10 15

Thr Glu Gly Val Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys
 20 25 30

Gly Gln Pro Phe Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile
 35 40 45

Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg
 50 55 60

Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr
 65 70 75 80

Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg
 85 90 95

His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu
 100 105 110

Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp
 115 120 125

Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys
 130 135 140

- 208 -

Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
 145 150 155 160

Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr
 165 170 175

Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp
 180 185 190

Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg
 195 200 205

Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys
 210 215 220

Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser
 225 230 235 240

Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His
 245 250 255

Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile
 260 265 270

Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr
 275 280 285

Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu
 290 295 300

Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr
 305 310 315 320

Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro
 325 330 335

Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu
 340 345 350

Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr
 355 360 365

Ala Arg Phe Gln Pro Gly Val Leu Glu Ala Pro
 370 375

- 209 -

<210> 111

<211> 847

<212> PRT

<213> Homo sapiens

<400> 111

Met Glu Pro Leu Lys Ser Leu Phe Leu Lys Ser Pro Leu Gly Ser Trp
 1 5 10 15

Asn Gly Ser Gly Ser Gly Gly Gly Gly Gly Gly Gly Gly Arg Pro
 20 25 30

Glu Gly Ser Pro Lys Ala Ala Gly Tyr Ala Asn Pro Val Trp Thr Ala
 35 40 45

Leu Phe Asp Tyr Glu Pro Ser Gly Gln Asp Glu Leu Ala Leu Arg Lys
 50 55 60

Gly Asp Arg Val Glu Val Leu Ser Arg Asp Ala Ala Ile Ser Gly Asp
 65 70 75 80

Glu Gly Trp Trp Ala Gly Gln Val Gly Gly Gln Val Gly Ile Phe Pro
 85 90 95

Ser Asn Tyr Val Ser Arg Gly Gly Gly Pro Pro Pro Cys Glu Val Ala
 100 105 110

Ser Phe Gln Glu Leu Arg Leu Glu Glu Val Ile Gly Ile Gly Gly Phe
 115 120 125

Gly Lys Val Tyr Arg Gly Ser Trp Arg Gly Glu Leu Val Ala Val Lys
 130 135 140

Ala Ala Arg Gln Asp Pro Asp Glu Asp Ile Ser Val Thr Ala Glu Ser
 145 150 155 160

Val Arg Gln Glu Ala Arg Leu Phe Ala Met Leu Ala His Pro Asn Ile
 165 170 175

Ile Ala Leu Lys Ala Val Cys Leu Glu Glu Pro Asn Leu Cys Leu Val
 180 185 190

- 210 -

Met Glu Tyr Ala Ala Gly Gly Pro Leu Ser Arg Ala Leu Ala Gly Arg
195 200 205

Arg Val Pro Pro His Val Leu Val Asn Trp Ala Val Gln Ile Ala Arg
210 215 220

Gly Met His Tyr Leu His Cys Glu Ala Leu Val Pro Val Ile His Arg
225 230 235 240

Asp Leu Lys Ser Asn Asn Ile Leu Leu Leu Gln Pro Ile Glu Ser Asp
245 250 255

Asp Met Glu His Lys Thr Leu Lys Ile Thr Asp Phe Gly Leu Ala Arg
260 265 270

Glu Trp His Lys Thr Thr Gln Met Ser Ala Ala Gly Thr Tyr Ala Trp
275 280 285

Met Ala Pro Glu Val Ile Lys Ala Ser Thr Phe Ser Lys Gly Ser Asp
290 295 300

Val Trp Ser Phe Gly Val Leu Leu Trp Glu Leu Leu Thr Gly Glu Val
305 310 315 320

Pro Tyr Arg Gly Ile Asp Cys Leu Ala Val Ala Tyr Gly Val Ala Val
325 330 335

Asn Lys Leu Thr Leu Pro Ile Pro Ser Thr Cys Pro Glu Pro Phe Ala
340 345 350

Gln Leu Met Ala Asp Cys Trp Ala Gln Asp Pro His Arg Arg Pro Asp
355 360 365

Phe Ala Ser Ile Leu Gln Gln Leu Glu Ala Leu Glu Ala Gln Val Leu
370 375 380

Arg Glu Met Pro Arg Asp Ser Phe His Ser Met Gln Glu Gly Trp Lys
385 390 395 400

Arg Glu Ile Gln Gly Leu Phe Asp Glu Leu Arg Ala Lys Glu Lys Glu
405 410 415

Leu Leu Ser Arg Glu Glu Glu Leu Thr Arg Ala Ala Arg Glu Gln Arg

- 211 -

420	425	430
Ser Gln Ala Glu Gln Leu Arg Arg Arg Glu His Leu Leu Ala Gln Trp 435 440 445		
Glu Leu Glu Val Phe Glu Arg Glu Leu Thr Leu Leu Leu Gln Gln Val 450 455 460		
Asp Arg Glu Arg Pro His Val Arg Arg Arg Arg Gly Thr Phe Lys Arg 465 470 475 480		
Ser Lys Leu Arg Ala Arg Asp Gly Gly Glu Arg Ile Ser Met Pro Leu 485 490 495		
Asp Phe Lys His Arg Ile Thr Val Gln Ala Ser Pro Gly Leu Asp Arg 500 505 510		
Arg Arg Asn Val Phe Glu Val Gly Pro Gly Asp Ser Pro Thr Phe Pro 515 520 525		
Arg Phe Arg Ala Ile Gln Leu Glu Pro Ala Glu Pro Gly Gln Ala Trp 530 535 540		
Gly Arg Gln Ser Pro Arg Arg Leu Glu Asp Ser Ser Asn Gly Glu Arg 545 550 555 560		
Arg Ala Cys Trp Ala Trp Gly Pro Ser Ser Pro Lys Pro Gly Glu Ala 565 570 575		
Gln Asn Gly Arg Arg Arg Ser Arg Met Asp Glu Ala Thr Trp Tyr Leu 580 585 590		
Asp Ser Asp Asp Ser Ser Pro Leu Gly Ser Pro Ser Thr Pro Pro Ala 595 600 605		
Leu Asn Gly Asn Pro Pro Arg Pro Ser Leu Glu Pro Glu Glu Pro Lys 610 615 620		
Arg Pro Val Pro Ala Glu Arg Gly Ser Ser Ser Gly Thr Pro Lys Leu 625 630 635 640		
Ile Gln Arg Ala Leu Leu Arg Gly Thr Ala Leu Leu Ala Ser Leu Gly 645 650 655		

- 212 -

Leu Gly Arg Asp Leu Gln Pro Pro Gly Gly Pro Gly Arg Glu Arg Gly
660 665 670

Glu Ser Pro Thr Thr Pro Pro Thr Pro Thr Pro Ala Pro Cys Pro Thr
675 680 685

Glu Pro Pro Pro Ser Pro Leu Ile Cys Phe Ser Leu Lys Thr Pro Asp
690 695 700

Ser Pro Pro Thr Pro Ala Pro Leu Leu Leu Asp Leu Gly Ile Pro Val
705 710 715 720

Gly Gln Arg Ser Ala Lys Ser Pro Arg Arg Glu Glu Glu Pro Arg Gly
725 730 735

Gly Thr Val Ser Pro Pro Pro Gly Thr Ser Arg Ser Ala Pro Gly Thr
740 745 750

Pro Gly Thr Pro Arg Ser Pro Pro Leu Gly Leu Ile Ser Arg Pro Arg
755 760 765

Pro Ser Pro Leu Arg Ser Arg Ile Asp Pro Trp Ser Phe Val Ser Ala
770 775 780

Gly Pro Arg Pro Ser Pro Leu Pro Ser Pro Gln Pro Ala Pro Arg Arg
785 790 795 800

Ala Pro Trp Thr Leu Phe Pro Asp Ser Asp Pro Phe Trp Asp Ser Pro
805 810 815

Pro Ala Asn Pro Phe Gln Gly Gly Pro Gln Asp Cys Arg Ala Gln Thr
820 825 830

Lys Asp Met Gly Ala Gln Ala Pro Trp Val Pro Glu Ala Gly Pro
835 840 845

<210> 112

<211> 4544

<212> PRT

<213> Homo sapiens

<400> 112

- 213 -

Met Leu Thr Pro Pro Leu Leu Leu Leu Leu Pro Leu Leu Ser Ala Leu
 1 5 10 15
 Val Ala Ala Ala Ile Asp Ala Pro Lys Thr Cys Ser Pro Lys Gln Phe
 20 25 30
 Ala Cys Arg Asp Gln Ile Thr Cys Ile Ser Lys Gly Trp Arg Cys Asp
 35 40 45
 Gly Glu Arg Asp Cys Pro Asp Gly Ser Asp Glu Ala Pro Glu Ile Cys
 50 55 60
 Pro Gln Ser Lys Ala Gln Arg Cys Gln Pro Asn Glu His Asn Cys Leu
 65 70 75 80
 Gly Thr Glu Leu Cys Val Pro Met Ser Arg Leu Cys Asn Gly Val Gln
 85 90 95
 Asp Cys Met Asp Gly Ser Asp Glu Gly Pro His Cys Arg Glu Leu Gln
 100 105 110
 Gly Asn Cys Ser Arg Leu Gly Cys Gln His His Cys Val Pro Thr Leu
 115 120 125
 Asp Gly Pro Thr Cys Tyr Cys Asn Ser Ser Phe Gln Leu Gln Ala Asp
 130 135 140
 Gly Lys Thr Cys Lys Asp Phe Asp Glu Cys Ser Val Tyr Gly Thr Cys
 145 150 155 160
 Ser Gln Leu Cys Thr Asn Thr Asp Gly Ser Phe Ile Cys Gly Cys Val
 165 170 175
 Glu Gly Tyr Leu Leu Gln Pro Asp Asn Arg Ser Cys Lys Ala Lys Asn
 180 185 190
 Glu Pro Val Asp Arg Pro Pro Val Leu Leu Ile Ala Asn Ser Gln Asn
 195 200 205
 Ile Leu Ala Thr Tyr Leu Ser Gly Ala Gln Val Ser Thr Ile Thr Pro
 210 215 220
 Thr Ser Thr Arg Gln Thr Thr Ala Met Asp Phe Ser Tyr Ala Asn Glu
 225 230 235 240

Thr Val Cys Trp Val His Val Gly Asp Ser Ala Ala Gln Thr Gln Leu
245 250 255

Ile Asn Ile Ser Leu Ser Leu His His Val Glu Gln Met Ala Ile Asp
275 280 285

Phe Val Cys Asn Arg Asn Gly Asp Thr Cys Val Thr Leu Leu Asp Leu
305 310 315 320

Val Phe Phe Thr Asp Tyr Gly Gln Ile Pro Lys Val Glu Arg Cys Asp
340 345 350

Pro His Gly Ile Thr Leu Asp Leu Val Ser Arg Leu Val Tyr Trp Ala
370 375 380

Arg Gln Thr Ile Ile Gln Gly Ile Leu Ile Glu His Leu Tyr Gly Leu
405 410 415

Ala Gln Gln Lys Thr Ser Val Ile Arg Val Asn Arg Phe Asn Ser Thr
435 440 445

Tyr His Gln Arg Arg Gln Pro Arg Val Arg Ser His Ala Cys Glu Asn

- 215 -

465		470		475		480									
Asp	Gln	Tyr	Gly	Lys	Pro	Gly	Gly	Cys	Ser	Asp	Ile	Cys	Leu	Leu	Ala
				485					490					495	
Asn	Ser	His	Lys	Ala	Arg	Thr	Cys	Arg	Cys	Arg	Ser	Gly	Phe	Ser	Leu
			500					505					510		
Gly	Ser	Asp	Gly	Lys	Ser	Cys	Lys	Lys	Pro	Glu	His	Glu	Leu	Phe	Leu
		515					520					525			
Val	Tyr	Gly	Lys	Gly	Arg	Pro	Gly	Ile	Ile	Arg	Gly	Met	Asp	Met	Gly
	530					535					540				
Ala	Lys	Val	Pro	Asp	Glu	His	Met	Ile	Pro	Ile	Glu	Asn	Leu	Met	Asn
545					550					555					560
Pro	Arg	Ala	Leu	Asp	Phe	His	Ala	Glu	Thr	Gly	Phe	Ile	Tyr	Phe	Ala
				565					570					575	
Asp	Thr	Thr	Ser	Tyr	Leu	Ile	Gly	Arg	Gln	Lys	Ile	Asp	Gly	Thr	Glu
			580					585					590		
Arg	Glu	Thr	Ile	Leu	Lys	Asp	Gly	Ile	His	Asn	Val	Glu	Gly	Val	Ala
		595					600					605			
Val	Asp	Trp	Met	Gly	Asp	Asn	Leu	Tyr	Trp	Thr	Asp	Asp	Gly	Pro	Lys
	610					615					620				
Lys	Thr	Ile	Ser	Val	Ala	Arg	Leu	Glu	Lys	Ala	Ala	Gln	Thr	Arg	Lys
625					630					635					640
Thr	Leu	Ile	Glu	Gly	Lys	Met	Thr	His	Pro	Arg	Ala	Ile	Val	Val	Asp
				645					650					655	
Pro	Leu	Asn	Gly	Trp	Met	Tyr	Trp	Thr	Asp	Trp	Glu	Glu	Asp	Pro	Lys
			660					665					670		
Asp	Ser	Arg	Arg	Gly	Arg	Leu	Glu	Arg	Ala	Trp	Met	Asp	Gly	Ser	His
		675					680					685			
Arg	Asp	Ile	Phe	Val	Thr	Ser	Lys	Thr	Val	Leu	Trp	Pro	Asn	Gly	Leu
	690					695					700				

- 216 -

Ser Leu Asp Ile Pro Ala Gly Arg Leu Tyr Trp Val Asp Ala Phe Tyr
705 710 715 720

Asp Arg Ile Glu Thr Ile Leu Leu Asn Gly Thr Asp Arg Lys Ile Val
725 730 735

Tyr Glu Gly Pro Glu Leu Asn His Ala Phe Gly Leu Cys His His Gly
740 745 750

Asn Tyr Leu Phe Trp Thr Glu Tyr Arg Ser Gly Ser Val Tyr Arg Leu
755 760 765

Glu Arg Gly Val Gly Gly Ala Pro Pro Thr Val Thr Leu Leu Arg Ser
770 775 780

Glu Arg Pro Pro Ile Phe Glu Ile Arg Met Tyr Asp Ala Gln Gln Gln
785 790 795 800

Gln Val Gly Thr Asn Lys Cys Arg Val Asn Asn Gly Gly Cys Ser Ser
805 810 815

Leu Cys Leu Ala Thr Pro Gly Ser Arg Gln Cys Ala Cys Ala Glu Asp
820 825 830

Gln Val Leu Asp Ala Asp Gly Val Thr Cys Leu Ala Asn Pro Ser Tyr
835 840 845

Val Pro Pro Pro Gln Cys Gln Pro Gly Glu Phe Ala Cys Ala Asn Ser
850 855 860

Arg Cys Ile Gln Glu Arg Trp Lys Cys Asp Gly Asp Asn Asp Cys Leu
865 870 875 880

Asp Asn Ser Asp Glu Ala Pro Ala Leu Cys His Gln His Thr Cys Pro
885 890 895

Ser Asp Arg Phe Lys Cys Glu Asn Asn Arg Cys Ile Pro Asn Arg Trp
900 905 910

Leu Cys Asp Gly Asp Asn Asp Cys Gly Asn Ser Glu Asp Glu Ser Asn
915 920 925

Ala Thr Cys Ser Ala Arg Thr Cys Pro Pro Asn Gln Phe Ser Cys Ala
930 935 940

- 217 -

Ser Gly Arg Cys Ile Pro Ile Ser Trp Thr Cys Asp Leu Asp Asp Asp
945 950 955 960

Cys Gly Asp Arg Ser Asp Glu Ser Ala Ser Cys Ala Tyr Pro Thr Cys
965 970 975

Phe Pro Leu Thr Gln Phe Thr Cys Asn Asn Gly Arg Cys Ile Asn Ile
980 985 990

Asn Trp Arg Cys Asp Asn Asp Asn Asp Cys Gly Asp Asn Ser Asp Glu
995 1000 1005

Ala Gly Cys Ser His Ser Cys Ser Ser Thr Gln Phe Lys Cys Asn
1010 1015 1020

Ser Gly Arg Cys Ile Pro Glu His Trp Thr Cys Asp Gly Asp Asn
1025 1030 1035

Asp Cys Gly Asp Tyr Ser Asp Glu Thr His Ala Asn Cys Thr Asn
1040 1045 1050

Gln Ala Thr Arg Pro Pro Gly Gly Cys His Thr Asp Glu Phe Gln
1055 1060 1065

Cys Arg Leu Asp Gly Leu Cys Ile Pro Leu Arg Trp Arg Cys Asp
1070 1075 1080

Gly Asp Thr Asp Cys Met Asp Ser Ser Asp Glu Lys Ser Cys Glu
1085 1090 1095

Gly Val Thr His Val Cys Asp Pro Ser Val Lys Phe Gly Cys Lys
1100 1105 1110

Asp Ser Ala Arg Cys Ile Ser Lys Ala Trp Val Cys Asp Gly Asp
1115 1120 1125

Asn Asp Cys Glu Asp Asn Ser Asp Glu Glu Asn Cys Glu Ser Leu
1130 1135 1140

Ala Cys Arg Pro Pro Ser His Pro Cys Ala Asn Asn Thr Ser Val
1145 1150 1155

Cys Leu Pro Pro Asp Lys Leu Cys Asp Gly Asn Asp Asp Cys Gly
1160 1165 1170

- 218 -

Asp	Gly	Ser	Asp	Glu	Gly	Glu	Leu	Cys	Asp	Gln	Cys	Ser	Leu	Asn
1175						1180					1185			
Asn	Gly	Gly	Cys	Ser	His	Asn	Cys	Ser	Val	Ala	Pro	Gly	Glu	Gly
1190						1195					1200			
Ile	Val	Cys	Ser	Cys	Pro	Leu	Gly	Met	Glu	Leu	Gly	Pro	Asp	Asn
1205						1210					1215			
His	Thr	Cys	Gln	Ile	Gln	Ser	Tyr	Cys	Ala	Lys	His	Leu	Lys	Cys
1220						1225					1230			
Ser	Gln	Lys	Cys	Asp	Gln	Asn	Lys	Phe	Ser	Val	Lys	Cys	Ser	Cys
1235						1240					1245			
Tyr	Glu	Gly	Trp	Val	Leu	Glu	Pro	Asp	Gly	Glu	Ser	Cys	Arg	Ser
1250						1255					1260			
Leu	Asp	Pro	Phe	Lys	Pro	Phe	Ile	Ile	Phe	Ser	Asn	Arg	His	Glu
1265						1270					1275			
Ile	Arg	Arg	Ile	Asp	Leu	His	Lys	Gly	Asp	Tyr	Ser	Val	Leu	Val
1280						1285					1290			
Pro	Gly	Leu	Arg	Asn	Thr	Ile	Ala	Leu	Asp	Phe	His	Leu	Ser	Gln
1295						1300					1305			
Ser	Ala	Leu	Tyr	Trp	Thr	Asp	Val	Val	Glu	Asp	Lys	Ile	Tyr	Arg
1310						1315					1320			
Gly	Lys	Leu	Leu	Asp	Asn	Gly	Ala	Leu	Thr	Ser	Phe	Glu	Val	Val
1325						1330					1335			
Ile	Gln	Tyr	Gly	Leu	Ala	Thr	Pro	Glu	Gly	Leu	Ala	Val	Asp	Trp
1340						1345					1350			
Ile	Ala	Gly	Asn	Ile	Tyr	Trp	Val	Glu	Ser	Asn	Leu	Asp	Gln	Ile
1355						1360					1365			
Glu	Val	Ala	Lys	Leu	Asp	Gly	Thr	Leu	Arg	Thr	Thr	Leu	Leu	Ala
1370						1375					1380			

- 219 -

Gly	Asp	Ile	Glu	His	Pro	Arg	Ala	Ile	Ala	Leu	Asp	Pro	Arg	Asp
1385						1390					1395			
Gly	Ile	Leu	Phe	Trp	Thr	Asp	Trp	Asp	Ala	Ser	Leu	Pro	Arg	Ile
1400						1405					1410			
Glu	Ala	Ala	Ser	Met	Ser	Gly	Ala	Gly	Arg	Arg	Thr	Val	His	Arg
1415						1420					1425			
Glu	Thr	Gly	Ser	Gly	Gly	Trp	Pro	Asn	Gly	Leu	Thr	Val	Asp	Tyr
1430						1435					1440			
Leu	Glu	Lys	Arg	Ile	Leu	Trp	Ile	Asp	Ala	Arg	Ser	Asp	Ala	Ile
1445						1450					1455			
Tyr	Ser	Ala	Arg	Tyr	Asp	Gly	Ser	Gly	His	Met	Glu	Val	Leu	Arg
1460						1465					1470			
Gly	His	Glu	Phe	Leu	Ser	His	Pro	Phe	Ala	Val	Thr	Leu	Tyr	Gly
1475						1480					1485			
Gly	Glu	Val	Tyr	Trp	Thr	Asp	Trp	Arg	Thr	Asn	Thr	Leu	Ala	Lys
1490						1495					1500			
Ala	Asn	Lys	Trp	Thr	Gly	His	Asn	Val	Thr	Val	Val	Gln	Arg	Thr
1505						1510					1515			
Asn	Thr	Gln	Pro	Phe	Asp	Leu	Gln	Val	Tyr	His	Pro	Ser	Arg	Gln
1520						1525					1530			
Pro	Met	Ala	Pro	Asn	Pro	Cys	Glu	Ala	Asn	Gly	Gly	Gln	Gly	Pro
1535						1540					1545			
Cys	Ser	His	Leu	Cys	Leu	Ile	Asn	Tyr	Asn	Arg	Thr	Val	Ser	Cys
1550						1555					1560			
Ala	Cys	Pro	His	Leu	Met	Lys	Leu	His	Lys	Asp	Asn	Thr	Thr	Cys
1565						1570					1575			
Tyr	Glu	Phe	Lys	Lys	Phe	Leu	Leu	Tyr	Ala	Arg	Gln	Met	Glu	Ile
1580						1585					1590			
Arg	Gly	Val	Asp	Leu	Asp	Ala	Pro	Tyr	Tyr	Asn	Tyr	Ile	Ile	Ser
1595						1600					1605			

- 220 -

Phe	Thr	Val	Pro	Asp	Ile	Asp	Asn	Val	Thr	Val	Leu	Asp	Tyr	Asp
1610						1615					1620			
Ala	Arg	Glu	Gln	Arg	Val	Tyr	Trp	Ser	Asp	Val	Arg	Thr	Gln	Ala
1625						1630					1635			
Ile	Lys	Arg	Ala	Phe	Ile	Asn	Gly	Thr	Gly	Val	Glu	Thr	Val	Val
1640						1645					1650			
Ser	Ala	Asp	Leu	Pro	Asn	Ala	His	Gly	Leu	Ala	Val	Asp	Trp	Val
1655						1660					1665			
Ser	Arg	Asn	Leu	Phe	Trp	Thr	Ser	Tyr	Asp	Thr	Asn	Lys	Lys	Gln
1670						1675					1680			
Ile	Asn	Val	Ala	Arg	Leu	Asp	Gly	Ser	Phe	Lys	Asn	Ala	Val	Val
1685						1690					1695			
Gln	Gly	Leu	Glu	Gln	Pro	His	Gly	Leu	Val	Val	His	Pro	Leu	Arg
1700						1705					1710			
Gly	Lys	Leu	Tyr	Trp	Thr	Asp	Gly	Asp	Asn	Ile	Ser	Met	Ala	Asn
1715						1720					1725			
Met	Asp	Gly	Ser	Asn	Arg	Thr	Leu	Leu	Phe	Ser	Gly	Gln	Lys	Gly
1730						1735					1740			
Pro	Val	Gly	Leu	Ala	Ile	Asp	Phe	Pro	Glu	Ser	Lys	Leu	Tyr	Trp
1745						1750					1755			
Ile	Ser	Ser	Gly	Asn	His	Thr	Ile	Asn	Arg	Cys	Asn	Leu	Asp	Gly
1760						1765					1770			
Ser	Gly	Leu	Glu	Val	Ile	Asp	Ala	Met	Arg	Ser	Gln	Leu	Gly	Lys
1775						1780					1785			
Ala	Thr	Ala	Leu	Ala	Ile	Met	Gly	Asp	Lys	Leu	Trp	Trp	Ala	Asp
1790						1795					1800			
Gln	Val	Ser	Glu	Lys	Met	Gly	Thr	Cys	Ser	Lys	Ala	Asp	Gly	Ser
1805						1810					1815			
Gly	Ser	Val	Val	Leu	Arg	Asn	Ser	Thr	Thr	Leu	Val	Met	His	Met
1820						1825					1830			

- 221 -

Lys	Val	Tyr	Asp	Glu	Ser	Ile	Gln	Leu	Asp	His	Lys	Gly	Thr	Asn
1835						1840					1845			
Pro	Cys	Ser	Val	Asn	Asn	Gly	Asp	Cys	Ser	Gln	Leu	Cys	Leu	Pro
1850						1855					1860			
Thr	Ser	Glu	Thr	Thr	Arg	Ser	Cys	Met	Cys	Thr	Ala	Gly	Tyr	Ser
1865						1870					1875			
Leu	Arg	Ser	Gly	Gln	Gln	Ala	Cys	Glu	Gly	Val	Gly	Ser	Phe	Leu
1880						1885					1890			
Leu	Tyr	Ser	Val	His	Glu	Gly	Ile	Arg	Gly	Ile	Pro	Leu	Asp	Pro
1895						1900					1905			
Asn	Asp	Lys	Ser	Asp	Ala	Leu	Val	Pro	Val	Ser	Gly	Thr	Ser	Leu
1910						1915					1920			
Ala	Val	Gly	Ile	Asp	Phe	His	Ala	Glu	Asn	Asp	Thr	Ile	Tyr	Trp
1925						1930					1935			
Val	Asp	Met	Gly	Leu	Ser	Thr	Ile	Ser	Arg	Ala	Lys	Arg	Asp	Gln
1940						1945					1950			
Thr	Trp	Arg	Glu	Asp	Val	Val	Thr	Asn	Gly	Ile	Gly	Arg	Val	Glu
1955						1960					1965			
Gly	Ile	Ala	Val	Asp	Trp	Ile	Ala	Gly	Asn	Ile	Tyr	Trp	Thr	Asp
1970						1975					1980			
Gln	Gly	Phe	Asp	Val	Ile	Glu	Val	Ala	Arg	Leu	Asn	Gly	Ser	Phe
1985						1990					1995			
Arg	Tyr	Val	Val	Ile	Ser	Gln	Gly	Leu	Asp	Lys	Pro	Arg	Ala	Ile
2000						2005					2010			
Thr	Val	His	Pro	Glu	Lys	Gly	Tyr	Leu	Phe	Trp	Thr	Glu	Trp	Gly
2015						2020					2025			
Gln	Tyr	Pro	Arg	Ile	Glu	Arg	Ser	Arg	Leu	Asp	Gly	Thr	Glu	Arg
2030						2035					2040			

- 222 -

Val Val Leu Val Asn Val Ser Ile Ser Trp Pro Asn Gly Ile Ser
 2045 2050 2055

Val Asp Tyr Gln Asp Gly Lys Leu Tyr Trp Cys Asp Ala Arg Thr
 2060 2065 2070

Asp Lys Ile Glu Arg Ile Asp Leu Glu Thr Gly Glu Asn Arg Glu
 2075 2080 2085

Val Val Leu Ser Ser Asn Asn Met Asp Met Phe Ser Val Ser Val
 2090 2095 2100

Phe Glu Asp Phe Ile Tyr Trp Ser Asp Arg Thr His Ala Asn Gly
 2105 2110 2115

Ser Ile Lys Arg Gly Ser Lys Asp Asn Ala Thr Asp Ser Val Pro
 2120 2125 2130

Leu Arg Thr Gly Ile Gly Val Gln Leu Lys Asp Ile Lys Val Phe
 2135 2140 2145

Asn Arg Asp Arg Gln Lys Gly Thr Asn Val Cys Ala Val Ala Asn
 2150 2155 2160

Gly Gly Cys Gln Gln Leu Cys Leu Tyr Arg Gly Arg Gly Gln Arg
 2165 2170 2175

Ala Cys Ala Cys Ala His Gly Met Leu Ala Glu Asp Gly Ala Ser
 2180 2185 2190

Cys Arg Glu Tyr Ala Gly Tyr Leu Leu Tyr Ser Glu Arg Thr Ile
 2195 2200 2205

Leu Lys Ser Ile His Leu Ser Asp Glu Arg Asn Leu Asn Ala Pro
 2210 2215 2220

Val Gln Pro Phe Glu Asp Pro Glu His Met Lys Asn Val Ile Ala
 2225 2230 2235

Leu Ala Phe Asp Tyr Arg Ala Gly Thr Ser Pro Gly Thr Pro Asn
 2240 2245 2250

Arg Ile Phe Phe Ser Asp Ile His Phe Gly Asn Ile Gln Gln Ile
 2255 2260 2265

- 223 -

Asn	Asp	Asp	Gly	Ser	Arg	Arg	Ile	Thr	Ile	Val	Glu	Asn	Val	Gly
2270						2275					2280			
Ser	Val	Glu	Gly	Leu	Ala	Tyr	His	Arg	Gly	Trp	Asp	Thr	Leu	Tyr
2285						2290					2295			
Trp	Thr	Ser	Tyr	Thr	Thr	Ser	Thr	Ile	Thr	Arg	His	Thr	Val	Asp
2300						2305					2310			
Gln	Thr	Arg	Pro	Gly	Ala	Phe	Glu	Arg	Glu	Thr	Val	Ile	Thr	Met
2315						2320					2325			
Ser	Gly	Asp	Asp	His	Pro	Arg	Ala	Phe	Val	Leu	Asp	Glu	Cys	Gln
2330						2335					2340			
Asn	Leu	Met	Phe	Trp	Thr	Asn	Trp	Asn	Glu	Gln	His	Pro	Ser	Ile
2345						2350					2355			
Met	Arg	Ala	Ala	Leu	Ser	Gly	Ala	Asn	Val	Leu	Thr	Leu	Ile	Glu
2360						2365					2370			
Lys	Asp	Ile	Arg	Thr	Pro	Asn	Gly	Leu	Ala	Ile	Asp	His	Arg	Ala
2375						2380					2385			
Glu	Lys	Leu	Tyr	Phe	Ser	Asp	Ala	Thr	Leu	Asp	Lys	Ile	Glu	Arg
2390						2395					2400			
Cys	Glu	Tyr	Asp	Gly	Ser	His	Arg	Tyr	Val	Ile	Leu	Lys	Ser	Glu
2405						2410					2415			
Pro	Val	His	Pro	Phe	Gly	Leu	Ala	Val	Tyr	Gly	Glu	His	Ile	Phe
2420						2425					2430			
Trp	Thr	Asp	Trp	Val	Arg	Arg	Ala	Val	Gln	Arg	Ala	Asn	Lys	His
2435						2440					2445			
Val	Gly	Ser	Asn	Met	Lys	Leu	Leu	Arg	Val	Asp	Ile	Pro	Gln	Gln
2450						2455					2460			
Pro	Met	Gly	Ile	Ile	Ala	Val	Ala	Asn	Asp	Thr	Asn	Ser	Cys	Glu
2465						2470					2475			
Leu	Ser	Pro	Cys	Arg	Ile	Asn	Asn	Gly	Gly	Cys	Gln	Asp	Leu	Cys
2480						2485					2490			

- 224 -

Leu Leu Thr His Gln Gly His Val Asn Cys Ser Cys Arg Gly Gly
 2495 2500 2505

Arg Ile Leu Gln Asp Asp Leu Thr Cys Arg Ala Val Asn Ser Ser
 2510 2515 2520

Cys Arg Ala Gln Asp Glu Phe Glu Cys Ala Asn Gly Glu Cys Ile
 2525 2530 2535

Asn Phe Ser Leu Thr Cys Asp Gly Val Pro His Cys Lys Asp Lys
 2540 2545 2550

Ser Asp Glu Lys Pro Ser Tyr Cys Asn Ser Arg Arg Cys Lys Lys
 2555 2560 2565

Thr Phe Arg Gln Cys Ser Asn Gly Arg Cys Val Ser Asn Met Leu
 2570 2575 2580

Trp Cys Asn Gly Ala Asp Asp Cys Gly Asp Gly Ser Asp Glu Ile
 2585 2590 2595

Pro Cys Asn Lys Thr Ala Cys Gly Val Gly Glu Phe Arg Cys Arg
 2600 2605 2610

Asp Gly Thr Cys Ile Gly Asn Ser Ser Arg Cys Asn Gln Phe Val
 2615 2620 2625

Asp Cys Glu Asp Ala Ser Asp Glu Met Asn Cys Ser Ala Thr Asp
 2630 2635 2640

Cys Ser Ser Tyr Phe Arg Leu Gly Val Lys Gly Val Leu Phe Gln
 2645 2650 2655

Pro Cys Glu Arg Thr Ser Leu Cys Tyr Ala Pro Ser Trp Val Cys
 2660 2665 2670

Asp Gly Ala Asn Asp Cys Gly Asp Tyr Ser Asp Glu Arg Asp Cys
 2675 2680 2685

Pro Gly Val Lys Arg Pro Arg Cys Pro Leu Asn Tyr Phe Ala Cys
 2690 2695 2700

Pro Ser Gly Arg Cys Ile Pro Met Ser Trp Thr Cys Asp Lys Glu

- 225 -

2705	2710	2715
Asp Asp Cys Glu His Gly Glu 2720 2725	Asp Glu Thr His Cys 2730	Asn Lys Phe
Cys Ser Glu Ala Gln Phe Glu 2735 2740	Cys Gln Asn His Arg 2745	Cys Ile Ser
Lys Gln Trp Leu Cys Asp Gly 2750 2755	Ser Asp Asp Cys Gly 2760	Asp Gly Ser
Asp Glu Ala Ala His Cys Glu 2765 2770	Gly Lys Thr Cys Gly 2775	Pro Ser Ser
Phe Ser Cys Pro Gly Thr His 2780 2785	Val Cys Val Pro Glu 2790	Arg Trp Leu
Cys Asp Gly Asp Lys Asp Cys 2795 2800	Ala Asp Gly Ala Asp 2805	Glu Ser Ile
Ala Ala Gly Cys Leu Tyr Asn 2810 2815	Ser Thr Cys Asp Asp 2820	Arg Glu Phe
Met Cys Gln Asn Arg Gln Cys 2825 2830	Ile Pro Lys His Phe 2835	Val Cys Asp
His Asp Arg Asp Cys Ala Asp 2840 2845	Gly Ser Asp Glu Ser 2850	Pro Glu Cys
Glu Tyr Pro Thr Cys Gly Pro 2855 2860	Ser Glu Phe Arg Cys 2865	Ala Asn Gly
Arg Cys Leu Ser Ser Arg Gln 2870 2875	Trp Glu Cys Asp Gly 2880	Glu Asn Asp
Cys His Asp Gln Ser Asp Glu 2885 2890	Ala Pro Lys Asn Pro 2895	His Cys Thr
Ser Pro Glu His Lys Cys Asn 2900 2905	Ala Ser Ser Gln Phe 2910	Leu Cys Ser
Ser Gly Arg Cys Val Ala Glu 2915 2920	Ala Leu Leu Cys Asn 2925	Gly Gln Asp

- 226 -

Asp Cys Gly Asp Ser Ser Asp Glu Arg Gly Cys His Ile Asn Glu
2930 2935 2940

Cys Leu Ser Arg Lys Leu Ser Gly Cys Ser Gln Asp Cys Glu Asp
2945 2950 2955

Leu Lys Ile Gly Phe Lys Cys Arg Cys Arg Pro Gly Phe Arg Leu
2960 2965 2970

Lys Asp Asp Gly Arg Thr Cys Ala Asp Val Asp Glu Cys Ser Thr
2975 2980 2985

Thr Phe Pro Cys Ser Gln Arg Cys Ile Asn Thr His Gly Ser Tyr
2990 2995 3000

Lys Cys Leu Cys Val Glu Gly Tyr Ala Pro Arg Gly Gly Asp Pro
3005 3010 3015

His Ser Cys Lys Ala Val Thr Asp Glu Glu Pro Phe Leu Ile Phe
3020 3025 3030

Ala Asn Arg Tyr Tyr Leu Arg Lys Leu Asn Leu Asp Gly Ser Asn
3035 3040 3045

Tyr Thr Leu Leu Lys Gln Gly Leu Asn Asn Ala Val Ala Leu Asp
3050 3055 3060

Phe Asp Tyr Arg Glu Gln Met Ile Tyr Trp Thr Asp Val Thr Thr
3065 3070 3075

Gln Gly Ser Met Ile Arg Arg Met His Leu Asn Gly Ser Asn Val
3080 3085 3090

Gln Val Leu His Arg Thr Gly Leu Ser Asn Pro Asp Gly Leu Ala
3095 3100 3105

Val Asp Trp Val Gly Gly Asn Leu Tyr Trp Cys Asp Lys Gly Arg
3110 3115 3120

Asp Thr Ile Glu Val Ser Lys Leu Asn Gly Ala Tyr Arg Thr Val
3125 3130 3135

Leu Val Ser Ser Gly Leu Arg Glu Pro Arg Ala Leu Val Val Asp
3140 3145 3150

- 227 -

Val Gln Asn Gly Tyr Leu Tyr Trp Thr Asp Trp Gly Asp His Ser
3155 3160 3165

Leu Ile Gly Arg Ile Gly Met Asp Gly Ser Ser Arg Ser Val Ile
3170 3175 3180

Val Asp Thr Lys Ile Thr Trp Pro Asn Gly Leu Thr Leu Asp Tyr
3185 3190 3195

Val Thr Glu Arg Ile Tyr Trp Ala Asp Ala Arg Glu Asp Tyr Ile
3200 3205 3210

Glu Phe Ala Ser Leu Asp Gly Ser Asn Arg His Val Val Leu Ser
3215 3220 3225

Gln Asp Ile Pro His Ile Phe Ala Leu Thr Leu Phe Glu Asp Tyr
3230 3235 3240

Val Tyr Trp Thr Asp Trp Glu Thr Lys Ser Ile Asn Arg Ala His
3245 3250 3255

Lys Thr Thr Gly Thr Asn Lys Thr Leu Leu Ile Ser Thr Leu His
3260 3265 3270

Arg Pro Met Asp Leu His Val Phe His Ala Leu Arg Gln Pro Asp
3275 3280 3285

Val Pro Asn His Pro Cys Lys Val Asn Asn Gly Gly Cys Ser Asn
3290 3295 3300

Leu Cys Leu Leu Ser Pro Gly Gly Gly His Lys Cys Ala Cys Pro
3305 3310 3315

Thr Asn Phe Tyr Leu Gly Ser Asp Gly Arg Thr Cys Val Ser Asn
3320 3325 3330

Cys Thr Ala Ser Gln Phe Val Cys Lys Asn Asp Lys Cys Ile Pro
3335 3340 3345

Phe Trp Trp Lys Cys Asp Thr Glu Asp Asp Cys Gly Asp His Ser
3350 3355 3360

Asp Glu Pro Pro Asp Cys Pro Glu Phe Lys Cys Arg Pro Gly Gln
3365 3370 3375

- 228 -

Phe Gln Cys Ser Thr Gly Ile Cys Thr Asn Pro Ala Phe Ile Cys
3380 3385 3390

Asp Gly Asp Asn Asp Cys Gln Asp Asn Ser Asp Glu Ala Asn Cys
3395 3400 3405

Asp Ile His Val Cys Leu Pro Ser Gln Phe Lys Cys Thr Asn Thr
3410 3415 3420

Asn Arg Cys Ile Pro Gly Ile Phe Arg Cys Asn Gly Gln Asp Asn
3425 3430 3435

Cys Gly Asp Gly Glu Asp Glu Arg Asp Cys Pro Glu Val Thr Cys
3440 3445 3450

Ala Pro Asn Gln Phe Gln Cys Ser Ile Thr Lys Arg Cys Ile Pro
3455 3460 3465

Arg Val Trp Val Cys Asp Arg Asp Asn Asp Cys Val Asp Gly Ser
3470 3475 3480

Asp Glu Pro Ala Asn Cys Thr Gln Met Thr Cys Gly Val Asp Glu
3485 3490 3495

Phe Arg Cys Lys Asp Ser Gly Arg Cys Ile Pro Ala Arg Trp Lys
3500 3505 3510

Cys Asp Gly Glu Asp Asp Cys Gly Asp Gly Ser Asp Glu Pro Lys
3515 3520 3525

Glu Glu Cys Asp Glu Arg Thr Cys Glu Pro Tyr Gln Phe Arg Cys
3530 3535 3540

Lys Asn Asn Arg Cys Val Pro Gly Arg Trp Gln Cys Asp Tyr Asp
3545 3550 3555

Asn Asp Cys Gly Asp Asn Ser Asp Glu Glu Ser Cys Thr Pro Arg
3560 3565 3570

Pro Cys Ser Glu Ser Glu Phe Ser Cys Ala Asn Gly Arg Cys Ile
3575 3580 3585

Ala Gly Arg Trp Lys Cys Asp Gly Asp His Asp Cys Ala Asp Gly

- 229 -

3590		3595		3600
Ser Asp Glu Lys Asp Cys Thr Pro Arg Cys Asp Met Asp Gln Phe	3605	3610		3615
Gln Cys Lys Ser Gly His Cys Ile Pro Leu Arg Trp Arg Cys Asp	3620	3625		3630
Ala Asp Ala Asp Cys Met Asp Gly Ser Asp Glu Glu Ala Cys Gly	3635	3640		3645
Thr Gly Val Arg Thr Cys Pro Leu Asp Glu Phe Gln Cys Asn Asn	3650	3655		3660
Thr Leu Cys Lys Pro Leu Ala Trp Lys Cys Asp Gly Glu Asp Asp	3665	3670		3675
Cys Gly Asp Asn Ser Asp Glu Asn Pro Glu Glu Cys Ala Arg Phe	3680	3685		3690
Val Cys Pro Pro Asn Arg Pro Phe Arg Cys Lys Asn Asp Arg Val	3695	3700		3705
Cys Leu Trp Ile Gly Arg Gln Cys Asp Gly Thr Asp Asn Cys Gly	3710	3715		3720
Asp Gly Thr Asp Glu Glu Asp Cys Glu Pro Pro Thr Ala His Thr	3725	3730		3735
Thr His Cys Lys Asp Lys Lys Glu Phe Leu Cys Arg Asn Gln Arg	3740	3745		3750
Cys Leu Ser Ser Ser Leu Arg Cys Asn Met Phe Asp Asp Cys Gly	3755	3760		3765
Asp Gly Ser Asp Glu Glu Asp Cys Ser Ile Asp Pro Lys Leu Thr	3770	3775		3780
Ser Cys Ala Thr Asn Ala Ser Ile Cys Gly Asp Glu Ala Arg Cys	3785	3790		3795
Val Arg Thr Glu Lys Ala Ala Tyr Cys Ala Cys Arg Ser Gly Phe	3800	3805		3810

- 230 -

His	Thr	Val	Pro	Gly	Gln	Pro	Gly	Cys	Gln	Asp	Ile	Asn	Glu	Cys
3815						3820					3825			
Leu	Arg	Phe	Gly	Thr	Cys	Ser	Gln	Leu	Cys	Asn	Asn	Thr	Lys	Gly
3830						3835					3840			
Gly	His	Leu	Cys	Ser	Cys	Ala	Arg	Asn	Phe	Met	Lys	Thr	His	Asn
3845						3850					3855			
Thr	Cys	Lys	Ala	Glu	Gly	Ser	Glu	Tyr	Gln	Val	Leu	Tyr	Ile	Ala
3860						3865					3870			
Asp	Asp	Asn	Glu	Ile	Arg	Ser	Leu	Phe	Pro	Gly	His	Pro	His	Ser
3875						3880					3885			
Ala	Tyr	Glu	Gln	Ala	Phe	Gln	Gly	Asp	Glu	Ser	Val	Arg	Ile	Asp
3890						3895					3900			
Ala	Met	Asp	Val	His	Val	Lys	Ala	Gly	Arg	Val	Tyr	Trp	Thr	Asn
3905						3910					3915			
Trp	His	Thr	Gly	Thr	Ile	Ser	Tyr	Arg	Ser	Leu	Pro	Pro	Ala	Ala
3920						3925					3930			
Pro	Pro	Thr	Thr	Ser	Asn	Arg	His	Arg	Arg	Gln	Ile	Asp	Arg	Gly
3935						3940					3945			
Val	Thr	His	Leu	Asn	Ile	Ser	Gly	Leu	Lys	Met	Pro	Arg	Gly	Ile
3950						3955					3960			
Ala	Ile	Asp	Trp	Val	Ala	Gly	Asn	Val	Tyr	Trp	Thr	Asp	Ser	Gly
3965						3970					3975			
Arg	Asp	Val	Ile	Glu	Val	Ala	Gln	Met	Lys	Gly	Glu	Asn	Arg	Lys
3980						3985					3990			
Thr	Leu	Ile	Ser	Gly	Met	Ile	Asp	Glu	Pro	His	Ala	Ile	Val	Val
3995						4000					4005			
Asp	Pro	Leu	Arg	Gly	Thr	Met	Tyr	Trp	Ser	Asp	Trp	Gly	Asn	His
4010						4015					4020			
Pro	Lys	Ile	Glu	Thr	Ala	Ala	Met	Asp	Gly	Thr	Leu	Arg	Glu	Thr
4025						4030					4035			

- 231 -

Leu Val Gln Asp Asn Ile Gln Trp Pro Thr Gly Leu Ala Val Asp
 4040 4045 4050

Tyr His Asn Glu Arg Leu Tyr Trp Ala Asp Ala Lys Leu Ser Val
 4055 4060 4065

Ile Gly Ser Ile Arg Leu Asn Gly Thr Asp Pro Ile Val Ala Ala
 4070 4075 4080

Asp Ser Lys Arg Gly Leu Ser His Pro Phe Ser Ile Asp Val Phe
 4085 4090 4095

Glu Asp Tyr Ile Tyr Gly Val Thr Tyr Ile Asn Asn Arg Val Phe
 4100 4105 4110

Lys Ile His Lys Phe Gly His Ser Pro Leu Val Asn Leu Thr Gly
 4115 4120 4125

Gly Leu Ser His Ala Ser Asp Val Val Leu Tyr His Gln His Lys
 4130 4135 4140

Gln Pro Glu Val Thr Asn Pro Cys Asp Arg Lys Lys Cys Glu Trp
 4145 4150 4155

Leu Cys Leu Leu Ser Pro Ser Gly Pro Val Cys Thr Cys Pro Asn
 4160 4165 4170

Gly Lys Arg Leu Asp Asn Gly Thr Cys Val Pro Val Pro Ser Pro
 4175 4180 4185

Thr Pro Pro Pro Asp Ala Pro Arg Pro Gly Thr Cys Asn Leu Gln
 4190 4195 4200

Cys Phe Asn Gly Gly Ser Cys Phe Leu Asn Ala Arg Arg Gln Pro
 4205 4210 4215

Lys Cys Arg Cys Gln Pro Arg Tyr Thr Gly Asp Lys Cys Glu Leu
 4220 4225 4230

Asp Gln Cys Trp Glu His Cys Arg Asn Gly Gly Thr Cys Ala Ala
 4235 4240 4245

Ser Pro Ser Gly Met Pro Thr Cys Arg Cys Pro Thr Gly Phe Thr
 4250 4255 4260

- 232 -

Gly Pro Lys Cys Thr Gln Gln Val Cys Ala Gly Tyr Cys Ala Asn
4265 4270 4275

Asn Ser Thr Cys Thr Val Asn Gln Gly Asn Gln Pro Gln Cys Arg
4280 4285 4290

Cys Leu Pro Gly Phe Leu Gly Asp Arg Cys Gln Tyr Arg Gln Cys
4295 4300 4305

Ser Gly Tyr Cys Glu Asn Phe Gly Thr Cys Gln Met Ala Ala Asp
4310 4315 4320

Gly Ser Arg Gln Cys Arg Cys Thr Ala Tyr Phe Glu Gly Ser Arg
4325 4330 4335

Cys Glu Val Asn Lys Cys Ser Arg Cys Leu Glu Gly Ala Cys Val
4340 4345 4350

Val Asn Lys Gln Ser Gly Asp Val Thr Cys Asn Cys Thr Asp Gly
4355 4360 4365

Arg Val Ala Pro Ser Cys Leu Thr Cys Val Gly His Cys Ser Asn
4370 4375 4380

Gly Gly Ser Cys Thr Met Asn Ser Lys Met Met Pro Glu Cys Gln
4385 4390 4395

Cys Pro Pro His Met Thr Gly Pro Arg Cys Glu Glu His Val Phe
4400 4405 4410

Ser Gln Gln Gln Pro Gly His Ile Ala Ser Ile Leu Ile Pro Leu
4415 4420 4425

Leu Leu Leu Leu Leu Leu Val Leu Val Ala Gly Val Val Phe Trp
4430 4435 4440

Tyr Lys Arg Arg Val Gln Gly Ala Lys Gly Phe Gln His Gln Arg
4445 4450 4455

Met Thr Asn Gly Ala Met Asn Val Glu Ile Gly Asn Pro Thr Tyr
4460 4465 4470

Lys Met Tyr Glu Gly Gly Glu Pro Asp Asp Val Gly Gly Leu Leu

- 233 -

4475 4480 4485
 Asp Ala Asp Phe Ala Leu Asp Pro Asp Lys Pro Thr Asn Phe Thr
 4490 4495 4500

 Asn Pro Val Tyr Ala Thr Leu Tyr Met Gly Gly His Gly Ser Arg
 4505 4510 4515

 His Ser Leu Ala Ser Thr Asp Glu Lys Arg Glu Leu Leu Gly Arg
 4520 4525 4530

 Gly Pro Glu Asp Glu Ile Gly Asp Pro Leu Ala
 4535 4540

 <210> 113
 <211> 113
 <212> PRT
 <213> Homo sapiens

 <400> 113

 Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
 1 5 10 15

 Leu Ala Val Ser Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp
 20 25 30

 Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met
 35 40 45

 Gly Asp Leu Val Leu Thr Val Leu Ile Ala Leu Ala Val Tyr Phe Leu
 50 55 60

 Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Ala Thr Arg
 65 70 75 80

 Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly
 85 90 95

 Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln Arg Pro Tyr Tyr
 100 105 110

- 234 -

Lys

<210> 114

<211> 281

<212> PRT

<213> Homo sapiens

<400> 114

Met	Gly	His	Pro	Pro	Leu	Leu	Pro	Leu	Leu	Leu	Leu	Leu	His	Thr	Cys
1				5					10					15	

Val	Pro	Ala	Ser	Trp	Gly	Leu	Arg	Cys	Met	Gln	Cys	Lys	Thr	Asn	Gly
			20					25						30	

Asp	Cys	Arg	Val	Glu	Glu	Cys	Ala	Leu	Gly	Gln	Asp	Leu	Cys	Arg	Thr
		35					40					45			

Thr	Ile	Val	Arg	Leu	Trp	Glu	Glu	Gly	Glu	Glu	Leu	Glu	Leu	Val	Glu
	50					55					60				

Lys	Ser	Cys	Thr	His	Ser	Glu	Lys	Thr	Asn	Arg	Thr	Leu	Ser	Tyr	Arg
65					70					75					80

Thr	Gly	Leu	Lys	Ile	Thr	Ser	Leu	Thr	Glu	Val	Val	Cys	Gly	Leu	Asp
				85					90					95	

Leu	Cys	Asn	Gln	Gly	Asn	Ser	Gly	Arg	Ala	Val	Thr	Tyr	Ser	Arg	Ser
			100					105						110	

Arg	Tyr	Leu	Glu	Cys	Ile	Ser	Cys	Gly	Ser	Ser	Asp	Met	Ser	Cys	Glu
		115					120					125			

Arg	Gly	Arg	His	Gln	Ser	Leu	Gln	Cys	Arg	Ser	Pro	Glu	Glu	Gln	Cys
	130					135					140				

Leu	Asp	Val	Val	Thr	His	Trp	Ile	Gln	Glu	Gly	Glu	Glu	Gly	Arg	Pro
145					150					155					160

Lys	Asp	Asp	Arg	His	Leu	Arg	Gly	Cys	Gly	Tyr	Leu	Pro	Gly	Cys	Pro
				165					170					175	

- 235 -

Gly Ser Asn Gly Phe His Asn Asn Asp Thr Phe His Phe Leu Lys Cys
 180 185 190

Cys Asn Thr Thr Lys Cys Asn Glu Gly Pro Ile Leu Glu Leu Glu Asn
 195 200 205

Leu Pro Gln Asn Gly Arg Gln Cys Tyr Ser Cys Lys Gly Asn Ser Thr
 210 215 220

His Gly Cys Ser Ser Glu Glu Thr Phe Leu Ile Asp Cys Arg Gly Pro
 225 230 235 240

Met Asn Gln Cys Leu Val Ala Thr Gly Thr His Glu Arg Ser Leu Trp
 245 250 255

Gly Ser Trp Leu Pro Cys Lys Ser Thr Thr Ala Leu Arg Pro Pro Cys
 260 265 270

Cys Glu Glu Ala Gln Ala Thr His Val
 275 280

<210> 115

<211> 351

<212> PRT

<213> Homo sapiens

<400> 115

Met Glu Thr Asn Phe Ser Thr Pro Leu Asn Glu Tyr Glu Glu Val Ser
 1 5 10 15

Tyr Glu Ser Ala Gly Tyr Thr Val Leu Arg Ile Leu Pro Leu Val Val
 20 25 30

Leu Gly Val Thr Phe Val Leu Gly Val Leu Gly Asn Gly Leu Val Ile
 35 40 45

Trp Val Ala Gly Phe Arg Met Thr Arg Thr Val Thr Thr Ile Cys Tyr
 50 55 60

Leu Asn Leu Ala Leu Ala Asp Phe Ser Phe Thr Ala Thr Leu Pro Phe
 65 70 75 80

- 236 -

Leu Ile Val Ser Met Ala Met Gly Glu Lys Trp Pro Phe Gly Trp Phe
85 90 95

Leu Cys Lys Leu Ile His Ile Val Val Asp Ile Asn Leu Phe Gly Ser
100 105 110

Val Phe Leu Ile Gly Phe Ile Ala Leu Asp Arg Cys Ile Cys Val Leu
115 120 125

His Pro Val Trp Ala Gln Asn His Arg Thr Val Ser Leu Ala Met Lys
130 135 140

Val Ile Val Gly Pro Trp Ile Leu Ala Leu Val Leu Thr Leu Pro Val
145 150 155 160

Phe Leu Phe Leu Thr Thr Val Thr Ile Pro Asn Gly Asp Thr Tyr Cys
165 170 175

Thr Phe Asn Phe Ala Ser Trp Gly Gly Thr Pro Glu Glu Arg Leu Lys
180 185 190

Val Ala Ile Thr Met Leu Thr Ala Arg Gly Ile Ile Arg Phe Val Ile
195 200 205

Gly Phe Ser Leu Pro Met Ser Ile Val Ala Ile Cys Tyr Gly Leu Ile
210 215 220

Ala Ala Lys Ile His Lys Lys Gly Met Ile Lys Ser Ser Arg Pro Leu
225 230 235 240

Arg Val Leu Thr Ala Val Val Ala Ser Phe Phe Ile Cys Trp Phe Pro
245 250 255

Phe Gln Leu Val Ala Leu Leu Gly Thr Val Trp Leu Lys Glu Met Leu
260 265 270

Phe Tyr Gly Lys Tyr Lys Ile Ile Asp Ile Leu Val Asn Pro Thr Ser
275 280 285

Ser Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Met Leu Tyr Val Phe
290 295 300

- 237 -

Val Gly Gln Asp Phe Arg Glu Arg Leu Ile His Ser Leu Pro Thr Ser
305 310 315 320

Leu Glu Arg Ala Leu Ser Glu Asp Ser Ala Pro Thr Asn Asp Thr Ala
325 330 335

Ala Asn Ser Ala Ser Pro Pro Ala Glu Thr Glu Leu Gln Ala Met
340 345 350

<210> 116

<211> 299

<212> PRT

<213> Homo sapiens

<400> 116

Met Arg Asp Arg Leu Pro Asp Leu Thr Ala Cys Arg Lys Asn Asp Asp
1 5 10 15

Gly Asp Thr Val Val Val Val Glu Lys Asp His Phe Met Asp Asp Phe
20 25 30

Phe His Gln Val Glu Glu Ile Arg Asn Ser Ile Asp Lys Ile Thr Gln
35 40 45

Tyr Val Glu Glu Val Lys Lys Asn His Ser Ile Ile Leu Ser Ala Pro
50 55 60

Asn Pro Glu Gly Lys Ile Lys Glu Glu Leu Glu Asp Leu Asn Lys Glu
65 70 75 80

Ile Lys Lys Thr Ala Asn Lys Ile Ala Ala Lys Leu Lys Ala Ile Glu
85 90 95

Gln Ser Phe Asp Gln Asp Glu Ser Gly Asn Arg Thr Ser Val Asp Leu
100 105 110

Arg Ile Arg Arg Thr Gln His Ser Val Leu Ser Arg Lys Phe Val Glu
115 120 125

Ala Met Ala Glu Tyr Asn Glu Ala Gln Thr Leu Phe Arg Glu Arg Ser
130 135 140

- 238 -

Lys Gly Arg Ile Gln Arg Gln Leu Glu Ile Thr Gly Arg Thr Thr Thr
145 150 155 160

Asp Asp Glu Leu Glu Glu Met Leu Glu Ser Gly Lys Pro Ser Ile Phe
165 170 175

Thr Ser Asp Ile Ile Ser Asp Ser Gln Ile Thr Arg Gln Ala Leu Asn
180 185 190

Glu Ile Glu Ser Arg His Lys Asp Ile Met Lys Leu Glu Thr Ser Ile
195 200 205

Arg Glu Leu His Glu Met Phe Met Asp Met Ala Met Phe Val Glu Thr
210 215 220

Gln Gly Glu Met Ile Asn Asn Ile Glu Arg Asn Val Met Asn Ala Thr
225 230 235 240

Asp Tyr Val Glu His Ala Lys Glu Glu Thr Lys Lys Ala Ile Lys Tyr
245 250 255

Gln Ser Lys Ala Arg Arg Lys Lys Trp Ile Ile Ile Ala Val Ser Val
260 265 270

Val Leu Val Val Tyr Arg Leu Phe Gly Leu Ser Leu Glu Tyr Val Val
275 280 285

Arg Ser Ala Ala Ser Leu Pro Gly Trp Gly Asn
290 295

<210> 117

<211> 836

<212> PRT

<213> Homo sapiens

<400> 117

Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1 5 10 15

Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
20 25 30

- 239 -

Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
35 40 45

Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
50 55 60

Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp
65 70 75 80

Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
85 90 95

Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
100 105 110

Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn
115 120 125

Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
130 135 140

Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145 150 155 160

Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
165 170 175

Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
180 185 190

Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
195 200 205

Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
210 215 220

Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225 230 235 240

Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
245 250 255

Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro

- 240 -

260					265					270					
Gln	Arg	Gly	Glu	Ala	Ser	Trp	Ala	Leu	Val	Gly	Pro	Leu	Pro	Leu	Glu
		275					280					285			
Ala	Leu	Gln	Tyr	Glu	Leu	Cys	Gly	Leu	Leu	Pro	Ala	Thr	Ala	Tyr	Thr
	290					295					300				
Leu	Gln	Ile	Arg	Cys	Ile	Arg	Trp	Pro	Leu	Pro	Gly	His	Trp	Ser	Asp
305						310					315				320
Trp	Ser	Pro	Ser	Leu	Glu	Leu	Arg	Thr	Thr	Glu	Arg	Ala	Pro	Thr	Val
				325					330					335	
Arg	Leu	Asp	Thr	Trp	Trp	Arg	Gln	Arg	Gln	Leu	Asp	Pro	Arg	Thr	Val
			340					345					350		
Gln	Leu	Phe	Trp	Lys	Pro	Val	Pro	Leu	Glu	Glu	Asp	Ser	Gly	Arg	Ile
		355					360					365			
Gln	Gly	Tyr	Val	Val	Ser	Trp	Arg	Pro	Ser	Gly	Gln	Ala	Gly	Ala	Ile
	370					375					380				
Leu	Pro	Leu	Cys	Asn	Thr	Thr	Glu	Leu	Ser	Cys	Thr	Phe	His	Leu	Pro
385						390					395				400
Ser	Glu	Ala	Gln	Glu	Val	Ala	Leu	Val	Ala	Tyr	Asn	Ser	Ala	Gly	Thr
				405					410					415	
Ser	Arg	Pro	Thr	Pro	Val	Val	Phe	Ser	Glu	Ser	Arg	Gly	Pro	Ala	Leu
			420					425					430		
Thr	Arg	Leu	His	Ala	Met	Ala	Arg	Asp	Pro	His	Ser	Leu	Trp	Val	Gly
		435					440					445			
Trp	Glu	Pro	Pro	Asn	Pro	Trp	Pro	Gln	Gly	Tyr	Val	Ile	Glu	Trp	Gly
	450					455					460				
Leu	Gly	Pro	Pro	Ser	Ala	Ser	Asn	Ser	Asn	Lys	Thr	Trp	Arg	Met	Glu
465						470					475				480
Gln	Asn	Gly	Arg	Ala	Thr	Gly	Phe	Leu	Leu	Lys	Glu	Asn	Ile	Arg	Pro
				485					490					495	

- 241 -

Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
 500 505 510

Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
 515 520 525

His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln
 530 535 540

Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
 545 550 555 560

His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
 565 570 575

Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
 580 585 590

Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
 595 600 605

Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
 610 615 620

Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Thr
 625 630 635 640

Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
 645 650 655

Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
 660 665 670

Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu
 675 680 685

Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys
 690 695 700

Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu
 705 710 715 720

Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val
 725 730 735

- 242 -

Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr
740 745 750

Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu
755 760 765

Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro
770 775 780

Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu
785 790 795 800

Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu
805 810 815

Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val His Gly Met Glu Ala
820 825 830

Leu Gly Ser Phe
835

<210> 118

<211> 540

<212> PRT

<213> Homo sapiens

<400> 118

Met Arg Val Ala Ala Ala Thr Ala Ala Ala Gly Ala Gly Pro Ala Met
1 5 10 15

Ala Val Trp Thr Arg Ala Thr Lys Ala Gly Leu Val Glu Leu Leu Leu
20 25 30

Arg Glu Arg Trp Val Arg Val Val Ala Glu Leu Ser Gly Glu Ser Leu
35 40 45

Ser Leu Thr Gly Asp Ala Ala Ala Ala Glu Leu Glu Pro Ala Leu Gly
50 55 60

Pro Ala Ala Ala Ala Phe Asn Gly Leu Pro Asn Gly Gly Gly Ala Gly
65 70 75 80

- 243 -

Asp Ser Leu Pro Gly Ser Pro Ser Arg Gly Leu Gly Pro Pro Ser Pro
85 90 95

Pro Ala Pro Pro Arg Gly Pro Ala Gly Glu Ala Gly Ala Ser Pro Pro
100 105 110

Val Arg Arg Val Arg Val Val Lys Gln Glu Ala Gly Gly Leu Gly Ile
115 120 125

Ser Ile Lys Gly Gly Arg Glu Asn Arg Met Pro Ile Leu Ile Ser Lys
130 135 140

Ile Phe Pro Gly Leu Ala Ala Asp Gln Ser Arg Ala Leu Arg Leu Gly
145 150 155 160

Asp Ala Ile Leu Ser Val Asn Gly Thr Asp Leu Arg Gln Ala Thr His
165 170 175

Asp Gln Ala Val Gln Ala Leu Lys Arg Ala Gly Lys Glu Val Leu Leu
180 185 190

Glu Val Lys Phe Ile Arg Glu Val Thr Pro Tyr Ile Lys Lys Pro Ser
195 200 205

Leu Val Ser Asp Leu Pro Trp Glu Gly Ala Ala Pro Gln Ser Pro Ser
210 215 220

Phe Ser Gly Ser Glu Asp Ser Gly Ser Pro Lys His Gln Asn Ser Thr
225 230 235 240

Lys Asp Arg Lys Ile Ile Pro Leu Lys Met Cys Phe Ala Ala Arg Asn
245 250 255

Leu Ser Met Pro Asp Leu Glu Asn Arg Leu Ile Glu Leu His Ser Pro
260 265 270

Asp Ser Arg Asn Thr Leu Ile Leu Arg Cys Lys Asp Thr Ala Thr Ala
275 280 285

His Ser Trp Phe Val Ala Ile His Thr Asn Ile Met Ala Leu Leu Pro
290 295 300

Gln Val Leu Ala Glu Leu Asn Ala Met Leu Gly Ala Thr Ser Thr Ala

- 244 -

305		310		315		320									
Gly	Gly	Ser	Lys	Glu	Val	Lys	His	Ile	Ala	Trp	Leu	Ala	Glu	Gln	Ala
				325					330					335	
Lys	Leu	Asp	Gly	Gly	Arg	Gln	Gln	Trp	Arg	Pro	Val	Leu	Met	Ala	Val
			340					345					350		
Thr	Glu	Lys	Asp	Leu	Leu	Leu	Tyr	Asp	Cys	Met	Pro	Trp	Thr	Arg	Asp
		355					360					365			
Ala	Trp	Ala	Ser	Pro	Cys	His	Ser	Tyr	Pro	Leu	Val	Ala	Thr	Arg	Leu
	370					375					380				
Val	His	Ser	Gly	Ser	Gly	Cys	Arg	Ser	Pro	Ser	Leu	Gly	Ser	Asp	Leu
385					390					395					400
Thr	Phe	Ala	Thr	Arg	Thr	Gly	Ser	Arg	Gln	Gly	Ile	Glu	Met	His	Leu
				405					410					415	
Phe	Arg	Val	Glu	Thr	His	Arg	Asp	Leu	Ser	Ser	Trp	Thr	Arg	Ile	Leu
			420					425					430		
Val	Gln	Gly	Cys	His	Ala	Ala	Ala	Glu	Leu	Ile	Lys	Glu	Val	Ser	Leu
		435					440					445			
Gly	Cys	Met	Leu	Asn	Gly	Gln	Glu	Val	Arg	Leu	Thr	Ile	His	Tyr	Glu
	450					455					460				
Asn	Gly	Phe	Thr	Ile	Ser	Arg	Glu	Asn	Gly	Gly	Ser	Ser	Ser	Ile	Leu
465					470					475					480
Tyr	Arg	Tyr	Pro	Phe	Glu	Arg	Leu	Lys	Met	Ser	Ala	Asp	Asp	Gly	Ile
				485					490					495	
Arg	Asn	Leu	Tyr	Leu	Asp	Phe	Gly	Gly	Pro	Glu	Gly	Glu	Leu	Thr	Met
			500					505					510		
Asp	Leu	His	Ser	Cys	Pro	Lys	Pro	Ile	Val	Phe	Val	Leu	His	Thr	Phe
		515					520					525			
Leu	Ser	Ala	Lys	Val	Thr	Arg	Met	Gly	Leu	Leu	Val				
		530				535					540				

- 245 -

<210> 119

<211> 250

<212> PRT

<213> Homo sapiens

<400> 119

Met Ala Asp Asn Phe Ser Leu His Asp Ala Leu Ser Gly Ser Gly Asn
 1 5 10 15

Pro Asn Pro Gln Gly Trp Pro Gly Ala Trp Gly Asn Gln Pro Ala Gly
 20 25 30

Ala Gly Gly Tyr Pro Gly Ala Ser Tyr Pro Gly Ala Tyr Pro Gly Gln
 35 40 45

Ala Pro Pro Gly Ala Tyr Pro Gly Gln Ala Pro Pro Gly Ala Tyr Pro
 50 55 60

Gly Ala Pro Gly Ala Tyr Pro Gly Ala Pro Ala Pro Gly Val Tyr Pro
 65 70 75 80

Gly Pro Pro Ser Gly Pro Gly Ala Tyr Pro Ser Ser Gly Gln Pro Ser
 85 90 95

Ala Thr Gly Ala Tyr Pro Ala Thr Gly Pro Tyr Gly Ala Pro Ala Gly
 100 105 110

Pro Leu Ile Val Pro Tyr Asn Leu Pro Leu Pro Gly Gly Val Val Pro
 115 120 125

Arg Met Leu Ile Thr Ile Leu Gly Thr Val Lys Pro Asn Ala Asn Arg
 130 135 140

Ile Ala Leu Asp Phe Gln Arg Gly Asn Asp Val Ala Phe His Phe Asn
 145 150 155 160

Pro Arg Phe Asn Glu Asn Asn Arg Arg Val Ile Val Cys Asn Thr Lys
 165 170 175

Leu Asp Asn Asn Trp Gly Arg Glu Glu Arg Gln Ser Val Phe Pro Phe
 180 185 190

- 246 -

Glu Ser Gly Lys Pro Phe Lys Ile Gln Val Leu Val Glu Pro Asp His
195 200 205

Phe Lys Val Ala Val Asn Asp Ala His Leu Leu Gln Tyr Asn His Arg
210 215 220

Val Lys Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile
225 230 235 240

Asp Leu Thr Ser Ala Ser Tyr Thr Met Ile
245 250

<210> 120

<211> 545

<212> PRT

<213> Homo sapiens

<400> 120

Met Asp Trp Gly Thr Glu Leu Trp Asp Gln Phe Glu Val Leu Glu Arg
1 5 10 15

His Thr Gln Trp Gly Leu Asp Leu Leu Asp Arg Tyr Val Lys Phe Val
20 25 30

Lys Glu Arg Thr Glu Val Glu Gln Ala Tyr Ala Lys Gln Leu Arg Ser
35 40 45

Leu Val Lys Lys Tyr Leu Pro Lys Arg Pro Ala Lys Asp Asp Pro Glu
50 55 60

Ser Lys Phe Ser Gln Gln Gln Ser Phe Val Gln Ile Leu Gln Glu Val
65 70 75 80

Asn Asp Phe Ala Gly Gln Arg Glu Leu Val Ala Glu Asn Leu Ser Val
85 90 95

Arg Val Cys Leu Glu Leu Thr Lys Tyr Ser Gln Glu Met Lys Gln Glu
100 105 110

Arg Lys Met His Phe Gln Glu Gly Arg Arg Ala Gln Gln Gln Leu Glu
115 120 125

- 247 -

Asn Gly Phe Lys Gln Leu Glu Asn Ser Lys Arg Lys Phe Glu Arg Asp
130 135 140

Cys Arg Glu Ala Glu Lys Ala Ala Gln Thr Ala Glu Arg Leu Asp Gln
145 150 155 160

Asp Ile Asn Ala Thr Lys Ala Asp Val Glu Lys Ala Lys Gln Gln Ala
165 170 175

His Leu Arg Ser His Met Ala Glu Glu Ser Lys Asn Glu Tyr Ala Ala
180 185 190

Gln Leu Gln Arg Phe Asn Arg Asp Gln Ala His Phe Tyr Phe Ser Gln
195 200 205

Met Pro Gln Ile Phe Asp Lys Leu Gln Asp Met Asp Glu Arg Arg Ala
210 215 220

Thr Arg Leu Gly Ala Gly Tyr Gly Leu Leu Ser Glu Ala Glu Leu Glu
225 230 235 240

Val Val Pro Ile Ile Ala Lys Cys Leu Glu Gly Met Lys Val Ala Ala
245 250 255

Asn Ala Val Asp Pro Lys Asn Asp Ser His Val Leu Ile Glu Leu His
260 265 270

Lys Ser Gly Phe Ala Arg Pro Gly Asp Val Glu Phe Glu Asp Phe Ser
275 280 285

Gln Pro Met Asn Arg Ala Pro Ser Asp Ser Ser Leu Gly Thr Pro Ser
290 295 300

Asp Gly Arg Pro Glu Leu Arg Gly Pro Gly Arg Ser Arg Thr Lys Arg
305 310 315 320

Trp Pro Phe Gly Lys Lys Asn Lys Thr Val Val Thr Glu Asp Phe Ser
325 330 335

His Leu Pro Pro Glu Gln Gln Arg Lys Arg Leu Gln Gln Gln Leu Glu
340 345 350

- 248 -

Glu Arg Ser Arg Glu Leu Gln Lys Glu Val Asp Gln Arg Glu Ala Leu
355 360 365

Lys Lys Met Lys Asp Val Tyr Glu Lys Thr Pro Gln Met Gly Asp Pro
370 375 380

Ala Ser Leu Glu Pro Gln Ile Ala Glu Thr Leu Ser Asn Ile Glu Arg
385 390 395 400

Leu Lys Leu Glu Val Gln Lys Tyr Glu Ala Trp Leu Ala Glu Ala Glu
405 410 415

Ser Arg Val Leu Ser Asn Arg Gly Asp Ser Leu Ser Arg His Ala Arg
420 425 430

Pro Pro Asp Pro Pro Ala Ser Ala Pro Pro Asp Ser Ser Ser Asn Ser
435 440 445

Ala Ser Gln Asp Thr Lys Glu Ser Ser Glu Glu Pro Pro Ser Glu Glu
450 455 460

Ser Gln Asp Thr Pro Ile Tyr Thr Glu Phe Asp Glu Asp Phe Glu Glu
465 470 475 480

Glu Pro Thr Ser Pro Ile Gly His Cys Val Ala Ile Tyr His Phe Glu
485 490 495

Gly Ser Ser Glu Gly Thr Ile Ser Met Ala Glu Gly Glu Asp Leu Ser
500 505 510

Leu Met Glu Glu Asp Lys Gly Asp Gly Trp Thr Arg Val Arg Arg Lys
515 520 525

Glu Gly Gly Glu Gly Tyr Val Pro Thr Ser Tyr Leu Arg Val Thr Leu
530 535 540

- 249 -

Asn
545

<210> 121

<211> 381

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<222> (59) .. (59)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (300) .. (300)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (318) .. (318)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (330) .. (330)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

- 250 -

<222> (345) .. (345)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (352) .. (352)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (367) .. (367)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (369) .. (369)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (376) .. (376)

<223> Xaa=any amino acid

<220>

<221> MISC_FEATURE

<222> (378) .. (378)

<223> Xaa=any amino acid

<400> 121

Met 1	Trp	Arg	Ser	Leu 5	Gly	Leu	Ala	Leu	Ala 10	Leu	Cys	Leu	Leu	Pro 15	Ser
Gly	Gly	Thr	Glu 20	Ser	Gln	Asp	Gln	Ser 25	Ser	Leu	Cys	Lys	Gln 30	Pro	Pro
Ala	Trp	Ser 35	Ile	Arg	Asp	Gln	Asp 40	Pro	Met	Leu	Asn	Ser 45	Asn	Gly	Ser
Val	Thr 50	Val	Val	Ala	Leu	Leu 55	Gln	Ala	Ser	Xaa	Tyr 60	Leu	Cys	Ile	Ile
Glu 65	Ala	Ser	Lys	Leu	Glu 70	Asp	Leu	Arg	Val	Lys 75	Leu	Lys	Lys	Glu	Gly 80
Tyr	Ser	Asn	Ile	Ser 85	Tyr	Ile	Val	Val	Asn 90	His	Gln	Gly	Ile	Ser 95	Ser
Arg	Leu	Lys	Tyr 100	Thr	His	Leu	Lys	Asn 105	Lys	Val	Ser	Glu	His 110	Ile	Pro
Val	Tyr	Gln 115	Gln	Glu	Glu	Asn	Gln 120	Thr	Asp	Val	Trp	Thr 125	Leu	Leu	Asn
Gly	Ser 130	Lys	Asp	Asp	Phe	Leu 135	Ile	Tyr	Asp	Arg	Cys 140	Gly	Arg	Leu	Val
Tyr 145	His	Leu	Gly	Leu	Pro 150	Phe	Ser	Phe	Leu	Thr 155	Phe	Pro	Tyr	Val	Glu 160
Glu	Ala	Ile	Lys	Ile 165	Ala	Tyr	Cys	Glu	Lys 170	Lys	Cys	Gly	Asn	Cys 175	Ser
Leu	Thr	Thr	Leu 180	Lys	Asp	Glu	Asp	Phe 185	Cys	Lys	Arg	Val	Ser 190	Leu	Ala
Thr	Val	Asp 195	Lys	Thr	Val	Glu	Thr 200	Pro	Ser	Pro	His	Tyr 205	His	His	Glu
His	His 210	His	Asn	His	Gly	His 215	Gln	His	Leu	Gly	Ser 220	Ser	Glu	Leu	Ser
Glu 225	Asn	Gln	Gln	Pro	Gly 230	Ala	Pro	Asn	Ala	Pro 235	Thr	His	Pro	Ala	Pro 240

Pro Gly Leu His His His His Lys His Lys Gly Gln His Arg Gln Gly
245 250 255

His Pro Glu Asn Arg Asp Met Pro Ala Ser Glu Asp Leu Gln Asp Leu
260 265 270

Gln Lys Lys Leu Cys Arg Lys Arg Cys Ile Asn Gln Leu Leu Cys Lys
275 280 285

Leu Pro Thr Asp Ser Glu Leu Ala Pro Arg Ser Xaa Cys Cys His Cys
290 295 300

Arg His Leu Ile Phe Glu Lys Thr Gly Ser Ala Ile Thr Xaa Gln Cys
305 310 315 320

Lys Glu Asn Leu Pro Ser Leu Cys Ser Xaa Gln Gly Leu Arg Ala Glu
325 330 335

Glu Asn Ile Thr Glu Ser Cys Gln Xaa Arg Leu Pro Pro Ala Ala Xaa
340 345 350

Gln Ile Ser Gln Gln Leu Ile Pro Thr Glu Ala Ser Ala Ser Xaa Arg
355 360 365

Xaa Lys Asn Gln Ala Lys Lys Xaa Glu Xaa Pro Ser Asn
370 375 380

<213> Homo sapiens

Met Val Asp Tyr His Ala Ala Asn Gln Ser Tyr Gln Tyr Gly Pro Ser
1 5 10 15

Ser Ala Ala Met Ala Trp Arg Arg Gly Ser Met Gly Asp Tyr Met Ala
20 25 30

BNSDOCID: <WO 03031650A2 | >

- 253 -

35					40					45					
Lys	Gln	Gln	Arg	Lys	Thr	Phe	Thr	Ala	Trp	Ser	Asn	Ser	His	Leu	Arg
50						55					60				
Lys	Ala	Gly	Thr	Gln	Ile	Glu	Asn	Ile	Asp	Glu	Asp	Phe	Arg	Asp	Gly
65					70					75					80
Leu	Lys	Leu	Met	Leu	Leu	Leu	Glu	Val	Ile	Ser	Gly	Glu	Arg	Leu	Pro
				85					90					95	
Lys	Pro	Glu	Arg	Gly	Lys	Met	Arg	Val	His	Lys	Ile	Asn	Asn	Val	Asn
			100					105					110		
Lys	Ala	Leu	Asp	Phe	Ile	Ala	Ser	Lys	Gly	Ile	Lys	Leu	Asp	Phe	His
	115						120					125			
Arg	Ala	Glu	Glu	Ile	Val	Asp	Gly	Asn	Ala	Lys	Met	Thr	Leu	Gly	Met
	130					135					140				
Ile	Trp	Thr	Ile	Ile	Leu	Arg	Phe	Ala	Ile	Gln	Asp	Ile	Ser	Val	Glu
145					150					155					160
Glu	Thr	Ser	Ala	Lys	Glu	Gly	Leu	Leu	Leu	Trp	Cys	Gln	Arg	Lys	Thr
				165					170					175	
Ala	Pro	Tyr	Lys	Asn	Val	Asn	Val	Gln	Asn	Phe	His	Ile	Ser	Trp	Lys
			180					185					190		
Asp	Gly	Leu	Ala	Phe	Asn	Ala	Leu	Ile	His	Arg	His	Arg	Pro	Glu	Leu
	195						200					205			
Ile	Glu	Tyr	Asp	Lys	Leu	Arg	Lys	Asp	Asp	Pro	Val	Thr	Asn	Leu	Asn
210						215					220				
Asn	Ala	Phe	Glu	Val	Ala	Glu	Lys	Tyr	Leu	Asp	Ile	Pro	Lys	Met	Leu
225						230					235				240
Asp	Ala	Glu	Asp	Ile	Val	Asn	Thr	Ala	Arg	Pro	Asp	Glu	Lys	Ala	Ile
				245					250					255	
Met	Thr	Tyr	Val	Ser	Ser	Phe	Tyr	His	Ala	Phe	Ser	Gly	Ala	Gln	Lys
			260					265					270		

- 254 -

Ala Glu Thr Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala Val
275 280 285

Asn Gln Glu Asn Cys Ser Thr Ser Met Glu Asp Tyr Glu Lys Leu Ala
290 295 300

Ser Asp Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asp
305 310 315 320

Arg Val Pro Gln Lys Thr Ile Gln Glu Met Gln Gln Lys Leu Glu Asp
325 330 335

Phe Arg Asp Tyr Arg Arg Val His Lys Pro Pro Lys Val Gln Glu Lys
340 345 350

Cys Gln Leu Glu Ile Asn Phe Asn Ser Val Gln Thr Lys Leu Arg Leu
355 360 365

Ser Asn Arg Pro Ala Phe Met Pro Ser Glu Gly Lys Met Val Ser Asp
370 375 380

Ile Asn Asn Gly Trp Gln His Leu Glu Gln Ala Glu Lys Gly Tyr Glu
385 390 395 400

Glu Trp Leu Leu Asn Glu Ile Arg Arg Leu Glu Arg Leu Asp His Leu
405 410 415

Ala Glu Lys Phe Arg Gln Lys Ala Ser Ile His Glu Ala Trp Thr Asp
420 425 430

Gly Lys Glu Ala Met Leu Lys His Arg Asp Tyr Glu Thr Ala Thr Leu
435 440 445

Ser Asp Ile Lys Ala Leu Ile Arg Lys His Glu Ala Phe Glu Ser Asp
450 455 460

Leu Ala Ala His Gln Asp Arg Val Glu Gln Ile Ala Ala Ser Ala Gln
465 470 475 480

Glu Leu Asn Glu Leu Asp Tyr Tyr Asp Ser His Asn Val Asn Thr Arg
485 490 495

Cys Gln Lys Ile Cys Asp Gln Trp Asp Ala Leu Gly Ser Leu Thr His
500 505 510

- 255 -

Ser Arg Arg Glu Ala Leu Glu Lys Thr Glu Lys Gln Leu Glu Ala Ile
515 520 525

Ile Asp Gln Leu His Leu Glu Tyr Ala Lys Pro Ala Ala Pro Phe Asn
530 535 540

Asn Trp Met Glu Ser Ala Met Glu Asp Leu Gln Asp Met Phe Ile Val
545 550 555 560

His Thr Ile Glu Glu Ile Glu Gly Leu Ile Ser Ala His Asp Gln Phe
565 570 575

Lys Ser Thr Leu Pro Asp Ala Asp Arg Glu Arg Glu Ala Ile Leu His
580 585 590

Pro Gln Gly Gly Gln Arg Ile Ala Glu Ser Asn His Ile Lys Leu Ser
595 600 605

Gly Ser Asn Pro Tyr Thr Thr Val Thr Pro Gln Ile Ile Asn Ser Lys
610 615 620

Trp Glu Lys Val Gln Gln Leu Val Pro Lys Arg Asp His Ala Leu Leu
625 630 635 640

Glu Glu Gln Ser Lys Gln Gln Gln Ser Asn Glu His Leu Arg Arg Gln
645 650 655

Phe Ala Ser Gln Ala Asn Val Val Gly Pro Trp Ile Gln Thr Lys Met
660 665 670

Glu Glu Ile Ala Ile Ser Ile Glu Met Asn Gly Thr Leu Glu Asp Gln
675 680 685

Leu Ser His Leu Lys Gln Tyr Glu Arg Ser Ile Val Asp Tyr Lys Pro
690 695 700

Asn Leu Asp Leu Leu Glu Gln Gln His Gln Leu Ile Gln Glu Ala Leu
705 710 715 720

Ile Phe Asp Asn Lys His Thr Asn Tyr Thr Met Glu His Ile Arg Val
725 730 735

Gly Trp Glu Gln Leu Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val
740 745 750

- 256 -

Glu Asn Gln Ile Leu Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln
755 760 765

Met Gln Glu Phe Arg Ala Ser Phe Asn His Phe Asp Lys Asp His Gly
770 775 780

Gly Ala Leu Gly Arg Gly Val Gln Gly Leu Pro His Gln Pro Gly Leu
785 790 795 800

Arg Arg Gly Glu Arg Pro Ala Gly Glu Ala Glu Phe Asn Arg Ile Met
805 810 815

Ser Leu Val Asp Pro Asn His Ser Gly Leu Val Thr Phe Gln Ala Phe
820 825 830

Ile Asp Phe Met Ser Arg Glu Thr Thr Asp Thr Asp Thr Ala Asp Gln
835 840 845

Val Ile Thr Ser Phe Lys Val Leu Ala Gly Asp Lys Asn Phe Ile Thr
850 855 860

Ala Glu Glu Leu Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys
865 870 875 880

Ile Ala Arg Met Ala Pro Tyr Gln Gly Pro Asp Gly Val Arg Gly Ala
885 890 895

Leu Asp Tyr Lys Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu
900 905 910

<210> 123

<211> 407

<212> PRT

<213> Homo sapiens

<400> 123

Phe Cys Pro Ala Val Leu Cys His Pro Asn Ser Pro Leu Asp Glu Glu
1 5 10 15

Asn Leu Thr Gln Glu Asn Gln Asp Arg Gly Thr His Val Asp Leu Gly

- 257 -

20					25					30					
Leu	Ala	Ser	Ala	Asn	Val	Asp	Phe	Ala	Phe	Ser	Leu	Tyr	Lys	Gln	Leu
		35					40					45			
Val	Leu	Lys	Ala	Pro	Asp	Lys	Asn	Val	Ile	Phe	Ser	Pro	Leu	Ser	Ile
	50					55					60				
Ser	Thr	Ala	Leu	Ala	Phe	Leu	Ser	Leu	Gly	Ala	His	Asn	Thr	Thr	Leu
65					70					75					80
Thr	Glu	Ile	Leu	Lys	Gly	Leu	Lys	Phe	Asn	Leu	Thr	Glu	Thr	Ser	Glu
				85					90					95	
Ala	Glu	Ile	His	Gln	Ser	Phe	Gln	His	Leu	Leu	Arg	Thr	Leu	Asn	Gln
			100					105					110		
Ser	Ser	Asp	Glu	Leu	Gln	Leu	Ser	Met	Gly	Asn	Ala	Met	Phe	Val	Lys
		115					120					125			
Glu	Gln	Leu	Ser	Leu	Leu	Asp	Arg	Phe	Thr	Glu	Asp	Ala	Lys	Arg	Leu
	130					135					140				
Tyr	Gly	Ser	Glu	Ala	Phe	Ala	Thr	Asp	Phe	Gln	Asp	Ser	Ala	Ala	Ala
145					150					155					160
Lys	Lys	Leu	Ile	Asn	Asp	Tyr	Val	Lys	Asn	Gly	Thr	Arg	Gly	Lys	Ile
				165					170					175	
Thr	Asp	Leu	Ile	Lys	Asp	Leu	Asp	Ser	Gln	Thr	Met	Met	Val	Leu	Val
			180					185					190		
Asn	Tyr	Ile	Phe	Phe	Lys	Ala	Lys	Trp	Glu	Met	Pro	Phe	Asp	Pro	Gln
		195					200					205			
Asp	Thr	His	Gln	Ser	Arg	Phe	Tyr	Leu	Ser	Lys	Lys	Lys	Trp	Val	Met
	210					215					220				
Val	Pro	Met	Met	Ser	Leu	His	His	Leu	Thr	Ile	Pro	Tyr	Phe	Arg	Asp
225					230					235					240
Glu	Glu	Leu	Ser	Cys	Thr	Val	Val	Glu	Leu	Lys	Tyr	Thr	Gly	Asn	Ala
				245					250					255	

- 258 -

Ser Ala Leu Phe Ile Leu Pro Asp Gln Asp Lys Met Glu Glu Val Glu
260 265 270

Ala Met Leu Leu Pro Glu Thr Leu Lys Arg Trp Arg Asp Ser Leu Glu
275 280 285

Phe Arg Glu Ile Gly Glu Leu Tyr Leu Pro Lys Phe Ser Ile Ser Arg
290 295 300

Asp Tyr Asn Leu Asn Asp Ile Leu Leu Gln Leu Gly Ile Glu Glu Ala
305 310 315 320

Phe Thr Ser Lys Ala Asp Leu Ser Gly Ile Thr Gly Ala Arg Asn Leu
325 330 335

Ala Val Ser Gln Val Val His Lys Ala Val Leu Asp Val Phe Glu Glu
340 345 350

Gly Thr Glu Ala Ser Ala Ala Thr Ala Val Lys Ile Thr Leu Leu Ser
355 360 365

Ala Leu Val Glu Thr Arg Thr Ile Val Arg Phe Asn Arg Pro Phe Leu
370 375 380

Met Ile Ile Val Pro Thr Asp Thr Gln Asn Ile Phe Phe Met Ser Lys
385 390 395 400

Val Thr Asn Pro Lys Gln Ala
405

<210> 124

<211> 451

<212> PRT

<213> Homo sapiens

<400> 124

Met Gly Lys Ser Phe Ala Asn Phe Met Cys Lys Lys Asp Phe His Pro
1 5 10 15

Ala Ser Lys Ser Asn Ile Lys Lys Val Trp Met Ala Glu Gln Lys Ile
20 25 30

- 259 -

Ser Tyr Asp Lys Lys Lys Gln Glu Glu Leu Met Gln Gln Tyr Leu Lys
 35 40 45

Glu Gln Glu Ser Tyr Asp Asn Arg Leu Leu Met Gly Asp Glu Arg Val
 50 55 60

Lys Asn Gly Leu Asn Phe Met Tyr Glu Ala Pro Pro Gly Ala Lys Lys
 65 70 75 80

Glu Asn Lys Glu Lys Glu Glu Thr Glu Gly Glu Thr Glu Tyr Lys Phe
 85 90 95

Glu Trp Gln Lys Gly Ala Pro Arg Glu Lys Tyr Ala Lys Asp Asp Met
 100 105 110

Asn Ile Arg Asp Gln Pro Phe Gly Ile Gln Val Arg Asn Val Arg Cys
 115 120 125

Ile Lys Cys His Lys Trp Val Met Ser Thr Gln Ile Glu Asn Val Leu
 130 135 140

Cys Leu Val Phe Leu Glu Val Asn Ala Ser Ser Val Pro Thr Asp Gly
 145 150 155 160

Ser Gly Pro Ser Met His Pro Ser Glu Leu Ile Gly Glu Met Arg Asn
 165 170 175

Gln Trp Val Cys Thr Glu Thr Lys Cys Thr Gly Glu Lys Leu Asp Arg
 180 185 190

Lys Leu Ile His His Arg Ser Met Leu Gln Val Gln Gly Glu Glu Asp
 195 200 205

Pro Glu Val Glu Phe Leu Lys Ser Leu Thr Thr Lys Gln Lys Gln Lys
 210 215 220

Leu Leu Arg Lys Leu Asp Arg Leu Glu Lys Lys Lys Lys Lys Asp
 225 230 235 240

Arg Lys Lys Lys Lys Phe Gln Lys Ser Arg Ser Lys His Lys Lys His
 245 250 255

Lys Ser Ser Ser Ser Tyr Leu Pro Pro Pro Pro Pro Leu Pro Leu Leu
 260 265 270

- 260 -

Arg Leu Gln Lys Ala Val Val Arg Val Arg Val Thr Ile Lys Lys Lys
275 280 285

Lys Leu Gln Arg Lys Lys Arg Lys Lys Asn Lys Cys Ser Gly His Asn
290 295 300

Asn Ser Asp Ser Glu Glu Lys Asp Lys Ser Lys Lys Arg Lys Leu His
305 310 315 320

Glu Glu Leu Ser Ser Thr His His Asn Arg Glu Lys Ala Lys Glu Lys
325 330 335

Pro Arg Phe Leu Lys His Glu Ser Ser Arg Glu Asp Ser Lys Trp Ser
340 345 350

His Ser Asp Ser Asp Lys Lys Ser Arg Thr His Lys His Ser Pro Glu
355 360 365

Lys Arg Gly Ser Glu Arg Lys Glu Gly Ser Ser Arg Ser His Gly Arg
370 375 380

Glu Glu Arg Ser Arg Arg Ser Gln Pro Glu Val Leu Val Val Thr Ser
385 390 395 400

Lys Gly Arg Gln Gly Asn Gly His Ser Glu His Pro Gly Glu Glu Gln
405 410 415

Ser Arg Arg Asn Asp Ser Arg Ser His Gly Thr Asp Leu Tyr Arg Gly
420 425 430

Glu Lys Met Tyr Arg Glu His Pro Gly Gly Thr His Thr Lys Val Thr
435 440 445

Gln Arg Glu
450

<210> 125

<211> 658

<212> PRT

<213> Homo sapiens

- 261 -

<400> 125

Met Ala Glu Ala Ala Ala Ala Gly Gly Thr Gly Leu Gly Ala Gly
 1 5 10 15

Ala Ser Tyr Gly Ser Ala Ala Asp Arg Asp Arg Asp Pro Asp Pro Asp
 20 25 30

Arg Ala Gly Arg Arg Leu Arg Val Leu Ser Gly His Leu Leu Gly Arg
 35 40 45

Pro Arg Glu Ala Leu Ser Thr Asn Glu Cys Lys Ala Arg Arg Ala Ala
 50 55 60

Ser Ala Ala Thr Ala Ala Pro Thr Ala Thr Pro Ala Ala Gln Glu Ser
 65 70 75 80

Gly Thr Ile Pro Lys Lys Arg Gln Glu Val Met Lys Trp Asn Gly Trp
 85 90 95

Gly Tyr Asn Asp Ser Lys Phe Ile Phe Asn Lys Lys Gly Gln Ile Glu
 100 105 110

Leu Thr Gly Lys Arg Tyr Pro Leu Ser Gly Met Gly Leu Pro Thr Phe
 115 120 125

Lys Glu Trp Ile Gln Asn Thr Leu Gly Val Asn Val Glu His Lys Thr
 130 135 140

Thr Ser Lys Ala Ser Leu Asn Pro Ser Asp Thr Pro Pro Ser Val Val
 145 150 155 160

Asn Glu Asp Phe Leu His Asp Leu Lys Glu Thr Asn Ile Ser Tyr Ser
 165 170 175

Gln Glu Ala Asp Asp Arg Val Phe Arg Ala His Gly His Cys Leu His
 180 185 190

Glu Ile Phe Leu Leu Arg Glu Gly Met Phe Glu Arg Ile Pro Asp Ile
 195 200 205

Val Leu Trp Pro Thr Cys His Asp Asp Val Val Lys Ile Val Asn Leu
 210 215 220

- 262 -

Ala Cys Lys Tyr Asn Leu Cys Ile Ile Pro Ile Gly Gly Gly Thr Ser
225 230 235 240

Val Ser Tyr Gly Leu Met Cys Pro Ala Asp Glu Thr Arg Thr Ile Ile
245 250 255

Ser Leu Asp Thr Ser Gln Met Asn Arg Ile Leu Trp Val Asp Glu Asn
260 265 270

Asn Leu Thr Ala His Val Glu Ala Gly Ile Thr Gly Gln Glu Leu Glu
275 280 285

Arg Gln Leu Lys Glu Ser Gly Tyr Cys Thr Gly His Glu Pro Asp Ser
290 295 300

Leu Glu Phe Ser Thr Val Gly Gly Trp Val Ser Thr Arg Ala Ser Gly
305 310 315 320

Met Lys Lys Asn Ile Tyr Gly Asn Ile Glu Asp Leu Val Val His Ile
325 330 335

Lys Met Val Thr Pro Arg Gly Ile Ile Glu Lys Ser Cys Gln Gly Pro
340 345 350

Arg Met Ser Thr Gly Pro Asp Ile His His Phe Ile Met Gly Ser Glu
355 360 365

Gly Thr Leu Gly Val Ile Thr Glu Ala Thr Ile Lys Ile Arg Pro Val
370 375 380

Pro Glu Tyr Gln Lys Tyr Gly Ser Val Ala Phe Pro Asn Phe Glu Gln
385 390 395 400

Gly Val Ala Cys Leu Arg Glu Ile Ala Lys Gln Arg Cys Ala Pro Ala
405 410 415

Ser Ile Arg Leu Met Asp Asn Lys Gln Phe Gln Phe Gly His Ala Leu
420 425 430

Lys Pro Gln Val Ser Ser Ile Phe Thr Ser Phe Leu Asp Gly Leu Lys
435 440 445

Lys Phe Tyr Ile Thr Lys Phe Lys Gly Phe Asp Pro Asn Gln Leu Ser
450 455 460

- 263 -

Val Ala Thr Leu Leu Phe Glu Gly Asp Arg Glu Lys Val Leu Gln His
465 470 475 480

Glu Lys Gln Val Tyr Asp Ile Ala Ala Lys Phe Gly Gly Leu Ala Ala
485 490 495

Gly Glu Asp Asn Gly Gln Arg Gly Tyr Leu Leu Thr Tyr Val Ile Ala
500 505 510

Tyr Ile Arg Asp Leu Ala Leu Glu Tyr Tyr Val Leu Gly Glu Ser Phe
515 520 525

Glu Thr Ser Ala Pro Trp Asp Arg Val Val Asp Leu Cys Arg Asn Val
530 535 540

Lys Glu Arg Ile Thr Arg Glu Cys Lys Glu Lys Gly Val Gln Phe Ala
545 550 555 560

Pro Phe Ser Thr Cys Arg Val Thr Gln Thr Tyr Asp Ala Gly Ala Cys
565 570 575

Ile Tyr Phe Tyr Phe Ala Phe Asn Tyr Arg Gly Ile Ser Asp Pro Leu
580 585 590

Thr Val Phe Glu Gln Thr Glu Ala Ala Ala Arg Glu Glu Ile Leu Ala
595 600 605

Asn Gly Gly Ser Leu Ser His His His Gly Val Gly Lys Leu Arg Lys
610 615 620

Gln Trp Leu Lys Glu Ser Ile Ser Asp Val Gly Phe Gly Met Leu Lys
625 630 635 640

Ser Val Lys Glu Tyr Val Asp Pro Asn Asn Ile Phe Gly Asn Arg Asn
645 650 655

Leu Leu

<210> 126

<211> 530

- 264 -

<212> PRT

<213> Homo sapiens

<400> 126

Met Arg Arg Leu Trp Gly Ala Ala Arg Lys Pro Ser Gly Ala Gly Trp
 1 5 10 15

Glu Lys Glu Trp Ala Glu Ala Pro Gln Glu Ala Pro Gly Ala Trp Ser
 20 25 30

Gly Arg Leu Gly Pro Gly Arg Ser Gly Arg Lys Gly Arg Ala Val Pro
 35 40 45

Gly Trp Ala Ser Trp Pro Ala His Leu Ala Leu Ala Ala Arg Pro Ala
 50 55 60

Arg His Leu Gly Gly Ala Gly Gln Gly Pro Arg Pro Leu His Ser Gly
 65 70 75 80

Thr Ala Pro Phe His Ser Arg Ala Ser Gly Glu Arg Gln Arg Arg Leu
 85 90 95

Glu Pro Gln Leu Gln His Glu Ser Arg Cys Arg Ser Ser Thr Pro Ala
 100 105 110

Asp Ala Trp Arg Ala Glu Ala Ala Leu Pro Val Arg Ala Met Gly Ala
 115 120 125

Pro Trp Gly Ser Pro Thr Ala Ala Ala Gly Gly Arg Arg Gly Trp Arg
 130 135 140

Arg Gly Arg Gly Leu Pro Trp Thr Val Cys Val Leu Ala Ala Ala Gly
 145 150 155 160

Leu Thr Cys Thr Ala Leu Ile Thr Tyr Ala Cys Trp Gly Gln Leu Pro
 165 170 175

Pro Leu Pro Trp Ala Ser Pro Thr Pro Ser Arg Pro Val Gly Val Leu
 180 185 190

Leu Trp Trp Glu Pro Phe Gly Gly Arg Asp Ser Ala Pro Arg Pro Pro
 195 200 205

- 265 -

Pro Asp Cys Arg Leu Arg Phe Asn Ile Ser Gly Cys Arg Leu Leu Thr
 210 215 220

Asp Arg Ala Ser Tyr Gly Glu Ala Gln Ala Val Leu Phe His His Arg
 225 230 235 240

Asp Leu Val Lys Gly Pro Pro Asp Trp Pro Pro Pro Trp Gly Ile Gln
 245 250 255

Ala His Thr Ala Glu Glu Val Asp Leu Arg Val Leu Asp Tyr Glu Glu
 260 265 270

Ala Ala Ala Ala Ala Glu Ala Leu Ala Thr Ser Ser Pro Arg Pro Pro
 275 280 285

Gly Gln Arg Trp Val Trp Met Asn Phe Glu Ser Pro Ser His Ser Pro
 290 295 300

Gly Leu Arg Ser Leu Ala Ser Asn Leu Phe Asn Trp Thr Leu Ser Tyr
 305 310 315 320

Arg Ala Asp Ser Asp Val Phe Val Pro Tyr Gly Tyr Leu Tyr Pro Arg
 325 330 335

Ser His Pro Gly Asp Pro Pro Ser Gly Leu Ala Pro Pro Leu Ser Arg
 340 345 350

Lys Gln Gly Leu Val Ala Trp Val Val Ser His Trp Asp Glu Arg Gln
 355 360 365

Ala Arg Val Arg Tyr Tyr His Gln Leu Ser Gln His Val Thr Val Asp
 370 375 380

Val Phe Gly Arg Gly Gly Pro Gly Gln Pro Val Pro Glu Ile Gly Leu
 385 390 395 400

Leu His Thr Val Ala Arg Tyr Lys Phe Tyr Leu Ala Phe Glu Asn Ser
 405 410 415

Gln His Leu Asp Tyr Ile Thr Glu Lys Leu Trp Arg Asn Ala Leu Leu
 420 425 430

Ala Gly Ala Val Pro Val Val Leu Gly Pro Asp Arg Ala Asn Tyr Glu
 435 440 445

- 266 -

Arg Phe Val Pro Arg Gly Ala Phe Ile His Val Asp Asp Phe Pro Ser
450 455 460

Ala Ser Ser Leu Ala Ser Tyr Leu Leu Phe Leu Asp Arg Asn Pro Ala
465 470 475 480

Val Tyr Arg Arg Tyr Phe His Trp Arg Arg Ser Tyr Ala Val His Ile
485 490 495

Thr Ser Phe Trp Asp Glu Pro Trp Cys Arg Val Cys Gln Ala Val Gln
500 505 510

Arg Ala Gly Asp Arg Pro Lys Ser Ile Arg Asn Leu Ala Ser Trp Phe
515 520 525

Glu Arg
530

<210> 127

<211> 541

<212> PRT

<213> Homo sapiens

<400> 127

Met Lys Ser Tyr Thr Pro Tyr Phe Ile Leu Leu Trp Ser Ala Val Gly
1 5 10 15

Ile Ala Lys Ala Ala Lys Ile Ile Ile Val Pro Pro Ile Met Phe Glu
20 25 30

Ser His Met Tyr Ile Phe Lys Thr Leu Ala Ser Ala Leu His Glu Arg
35 40 45

Gly His His Thr Val Phe Leu Leu Ser Glu Gly Arg Asp Ile Ala Pro
50 55 60

Ser Asn His Tyr Ser Leu Gln Arg Tyr Pro Gly Ile Phe Asn Ser Thr
65 70 75 80

Thr Ser Asp Ala Phe Leu Gln Ser Lys Met Arg Asn Ile Phe Ser Gly

- 267 -

85					90					95					
Arg	Leu	Thr	Ala	Ile	Glu	Leu	Phe	Asp	Ile	Leu	Asp	His	Tyr	Thr	Lys
			100					105					110		
Asn	Cys	Asp	Leu	Met	Val	Gly	Asn	His	Ala	Leu	Ile	Gln	Gly	Leu	Lys
		115					120					125			
Lys	Glu	Lys	Phe	Asp	Leu	Leu	Leu	Val	Asp	Pro	Asn	Asp	Met	Cys	Gly
	130					135					140				
Phe	Val	Ile	Ala	His	Leu	Leu	Gly	Val	Lys	Tyr	Ala	Val	Phe	Ser	Thr
145					150					155					160
Gly	Leu	Trp	Tyr	Pro	Ala	Glu	Val	Gly	Ala	Pro	Ala	Pro	Leu	Ala	Tyr
				165					170						175
Val	Pro	Glu	Phe	Asn	Ser	Leu	Leu	Thr	Asp	Arg	Met	Asn	Leu	Leu	Gln
			180					185					190		
Arg	Met	Lys	Asn	Thr	Gly	Val	Tyr	Leu	Ile	Ser	Arg	Leu	Gly	Val	Ser
		195					200					205			
Phe	Leu	Val	Leu	Pro	Lys	Tyr	Glu	Arg	Ile	Met	Gln	Lys	Tyr	Asn	Leu
	210					215					220				
Leu	Pro	Glu	Lys	Ser	Met	Tyr	Asp	Leu	Val	His	Gly	Ser	Ser	Leu	Trp
225					230					235					240
Met	Leu	Cys	Thr	Asp	Val	Ala	Leu	Glu	Phe	Pro	Arg	Pro	Thr	Leu	Pro
				245					250					255	
Asn	Val	Val	Tyr	Val	Gly	Gly	Ile	Leu	Thr	Lys	Pro	Ala	Ser	Pro	Leu
			260					265					270		
Pro	Glu	Asp	Leu	Gln	Arg	Trp	Val	Asn	Gly	Ala	Asn	Glu	His	Gly	Phe
		275					280					285			
Val	Leu	Val	Ser	Phe	Gly	Ala	Gly	Val	Lys	Tyr	Leu	Ser	Glu	Asp	Ile
	290					295					300				
Ala	Asn	Lys	Leu	Ala	Gly	Ala	Leu	Gly	Arg	Leu	Pro	Gln	Lys	Val	Ile
305					310					315					320

- 268 -

Trp Arg Phe Ser Gly Pro Lys Pro Lys Asn Leu Gly Asn Asn Thr Lys
325 330 335

Leu Ile Glu Trp Leu Pro Gln Asn Asp Leu Leu Gly His Ser Lys Ile
340 345 350

Lys Ala Phe Leu Ser His Gly Gly Leu Asn Ser Ile Phe Glu Thr Met
355 360 365

Tyr His Gly Val Pro Val Val Gly Ile Pro Leu Phe Gly Asp His Tyr
370 375 380

Asp Thr Met Thr Arg Val Gln Ala Lys Gly Met Gly Ile Leu Leu Glu
385 390 395 400

Trp Lys Thr Val Thr Glu Lys Glu Leu Tyr Glu Ala Leu Val Lys Val
405 410 415

Ile Asn Asn Pro Ser Tyr Arg Gln Arg Ala Gln Lys Leu Ser Glu Ile
420 425 430

His Lys Asp Gln Pro Gly His Pro Val Asn Arg Thr Ile Tyr Trp Ile
435 440 445

Asp Tyr Ile Ile Arg His Asn Gly Ala His His Leu Arg Ala Ala Val
450 455 460

His Gln Ile Ser Phe Cys Gln Tyr Phe Leu Leu Asp Ile Ala Phe Val
465 470 475 480

Leu Leu Leu Gly Ala Ala Leu Leu Tyr Phe Leu Leu Ser Trp Val Thr
485 490 495

Lys Phe Ile Tyr Arg Lys Ile Lys Ser Leu Trp Ser Arg Asn Lys His
500 505 510

Ser Thr Val Asn Gly His Tyr His Asn Gly Ile Leu Asn Gly Lys Tyr
515 520 525

Lys Arg Asn Gly His Ile Lys His Glu Lys Lys Val Lys
530 535 540

<210> 128

- 269 -

<211> 465

<212> PRT

<213> Homo sapiens

<400> 128

Met Ala Met Thr Gly Ser Thr Pro Cys Ser Ser Met Ser Asn His Thr
1 5 10 15

Lys Glu Arg Val Thr Met Thr Lys Val Thr Leu Glu Asn Phe Tyr Ser
20 25 30

Asn Leu Ile Ala Gln His Glu Glu Arg Glu Met Arg Gln Lys Lys Leu
35 40 45

Glu Lys Val Met Glu Glu Glu Gly Leu Lys Asp Glu Glu Lys Arg Leu
50 55 60

Arg Arg Ser Ala His Ala Arg Lys Glu Thr Glu Phe Leu Arg Leu Lys
65 70 75 80

Arg Thr Arg Leu Gly Leu Glu Asp Phe Glu Ser Leu Lys Val Ile Gly
85 90 95

Arg Gly Ala Phe Gly Glu Val Arg Leu Val Gln Lys Lys Asp Thr Gly
100 105 110

His Val Tyr Ala Met Lys Ile Leu Arg Lys Ala Asp Met Leu Glu Lys
115 120 125

Glu Gln Val Gly His Ile Arg Ala Glu Arg Asp Ile Leu Val Glu Ala
130 135 140

Asp Ser Leu Trp Val Val Lys Met Phe Tyr Ser Phe Gln Asp Lys Leu
145 150 155 160

Asn Leu Tyr Leu Ile Met Glu Phe Leu Pro Gly Gly Asp Met Met Thr
165 170 175

Leu Leu Met Lys Lys Asp Thr Leu Thr Glu Glu Glu Thr Gln Phe Tyr
180 185 190

Ile Ala Glu Thr Val Leu Ala Ile Asp Ser Ile His Gln Leu Gly Phe

- 270 -

195					200					205					
Ile	His	Arg	Asp	Ile	Lys	Pro	Asp	Asn	Leu	Leu	Leu	Asp	Ser	Lys	Gly
210						215					220				
His	Val	Lys	Leu	Ser	Asp	Phe	Gly	Leu	Cys	Thr	Gly	Leu	Lys	Lys	Ala
225					230					235					240
His	Arg	Thr	Glu	Phe	Tyr	Arg	Asn	Leu	Asn	His	Ser	Leu	Pro	Ser	Asp
				245					250					255	
Phe	Thr	Phe	Gln	Asn	Met	Asn	Ser	Lys	Arg	Lys	Ala	Glu	Thr	Trp	Lys
			260					265					270		
Arg	Asn	Arg	Arg	Gln	Leu	Ala	Phe	Ser	Thr	Val	Gly	Thr	Pro	Asp	Tyr
		275					280					285			
Ile	Ala	Pro	Glu	Val	Phe	Met	Gln	Thr	Gly	Tyr	Asn	Lys	Leu	Cys	Asp
290						295					300				
Trp	Trp	Ser	Leu	Gly	Val	Ile	Met	Tyr	Glu	Met	Leu	Ile	Gly	Tyr	Pro
305					310					315					320
Pro	Phe	Cys	Ser	Glu	Thr	Pro	Gln	Glu	Thr	Tyr	Lys	Lys	Val	Met	Asn
				325					330					335	
Trp	Lys	Glu	Thr	Leu	Thr	Phe	Pro	Pro	Glu	Val	Pro	Ile	Ser	Glu	Lys
			340					345					350		
Ala	Lys	Asp	Leu	Ile	Leu	Arg	Phe	Cys	Cys	Glu	Trp	Glu	His	Arg	Ile
		355					360					365			
Gly	Ala	Pro	Gly	Val	Glu	Glu	Ile	Lys	Ser	Asn	Ser	Phe	Phe	Glu	Gly
370						375					380				
Val	Asp	Trp	Glu	His	Ile	Arg	Glu	Arg	Pro	Ala	Ala	Ile	Ser	Ile	Glu
385					390					395					400
Ile	Lys	Ser	Ile	Asp	Asp	Thr	Ser	Asn	Phe	Asp	Glu	Phe	Pro	Glu	Ser
				405					410					415	
Asp	Ile	Leu	Lys	Pro	Thr	Val	Ala	Thr	Ser	Asn	His	Pro	Glu	Thr	Asp
			420					425					430		

- 271 -

Tyr Lys Asn Lys Asp Trp Val Phe Ile Asn Tyr Thr Tyr Lys Arg Phe
 435 440 445

Glu Gly Leu Thr Ala Arg Gly Ala Ile Pro Ser Tyr Met Lys Ala Ala
 450 455 460

Lys
 465

<210> 129

<211> 493

<212> PRT

<213> Homo sapiens

<400> 129

Met Ala Leu Phe Gly Ala Leu Phe Leu Ala Leu Leu Ala Gly Ala His
 1 5 10 15

Ala Glu Phe Pro Gly Cys Lys Ile Arg Val Thr Ser Lys Ala Leu Glu
 20 25 30

Leu Val Lys Gln Glu Gly Leu Arg Phe Leu Glu Gln Glu Leu Glu Thr
 35 40 45

Ile Thr Ile Pro Asp Leu Arg Gly Lys Glu Gly His Phe Tyr Tyr Asn
 50 55 60

Ile Ser Glu Val Lys Val Thr Glu Leu Gln Leu Thr Ser Ser Glu Leu
 65 70 75 80

Asp Phe Gln Pro Gln Gln Glu Leu Met Leu Gln Ile Thr Asn Ala Ser
 85 90 95

Leu Gly Leu Arg Phe Arg Arg Gln Leu Leu Tyr Trp Phe Phe Tyr Asp
 100 105 110

Gly Gly Tyr Ile Asn Ala Ser Ala Glu Gly Val Ser Ile Arg Thr Gly
 115 120 125

Leu Glu Leu Ser Arg Asp Pro Ala Gly Arg Met Lys Val Ser Asn Val
 130 135 140

- 272 -

Ser Cys Gln Ala Ser Val Ser Arg Met His Ala Ala Phe Gly Gly Thr
 145 150 155 160

Phe Lys Lys Val Tyr Asp Phe Leu Ser Thr Phe Ile Thr Ser Gly Met
 165 170 175

Arg Phe Leu Leu Asn Gln Gln Ile Cys Pro Val Leu Tyr His Ala Gly
 180 185 190

Thr Val Leu Leu Asn Ser Leu Leu Asp Thr Val Pro Val Arg Ser Ser
 195 200 205

Val Asp Glu Leu Val Gly Ile Asp Tyr Ser Leu Met Lys Asp Pro Val
 210 215 220

Ala Ser Thr Ser Asn Leu Asp Met Asp Phe Arg Gly Ala Phe Phe Pro
 225 230 235 240

Leu Thr Glu Arg Asn Trp Ser Leu Pro Asn Arg Ala Val Glu Pro Gln
 245 250 255

Leu Gln Glu Glu Glu Arg Met Val Tyr Val Ala Phe Ser Glu Phe Phe
 260 265 270

Phe Asp Ser Ala Met Glu Ser Tyr Phe Arg Ala Gly Ala Leu Gln Leu
 275 280 285

Leu Leu Val Gly Asp Lys Val Pro His Asp Leu Asp Met Leu Leu Arg
 290 295 300

Ala Thr Tyr Phe Gly Ser Ile Val Leu Leu Ser Pro Ala Val Ile Asp
 305 310 315 320

Ser Pro Leu Lys Leu Glu Leu Arg Val Leu Ala Pro Pro Arg Cys Thr
 325 330 335

Ile Lys Pro Ser Gly Thr Thr Ile Ser Val Thr Ala Ser Val Thr Ile
 340 345 350

Ala Leu Val Pro Pro Asp Gln Pro Glu Val Gln Leu Ser Ser Met Thr
 355 360 365

Met Asp Ala Arg Leu Ser Ala Lys Met Ala Leu Arg Gly Lys Ala Leu
 370 375 380

- 273 -

Arg Thr Gln Leu Asp Leu Arg Arg Phe Arg Ile Tyr Ser Asn His Ser
385 390 395 400

Ala Leu Glu Ser Leu Ala Leu Ile Pro Leu Gln Ala Pro Leu Lys Thr
405 410 415

Met Leu Gln Ile Gly Val Met Pro Met Leu Asn Glu Arg Thr Trp Arg
420 425 430

Gly Val Gln Ile Pro Leu Pro Glu Gly Ile Asn Phe Val His Glu Val
435 440 445

Val Thr Asn His Ala Gly Phe Leu Thr Ile Gly Ala Asp Leu His Phe
450 455 460

Ala Lys Gly Leu Arg Glu Val Ile Glu Lys Asn Arg Pro Ala Asp Val
465 470 475 480

Arg Ala Ser Thr Ala Pro Thr Pro Ser Thr Ala Ala Val
485 490

<210> 130

<211> 801

<212> PRT

<213> Homo sapiens

<400> 130

Leu Pro Leu His Ala Val Glu Lys Thr Gly Arg Pro Gly Gln Pro Ala
1 5 10 15

Leu Lys Met Pro Gly Lys Leu Arg Ser Asp Ala Gly Leu Glu Ser Asp
20 25 30

Thr Ala Met Lys Lys Gly Glu Thr Leu Arg Lys Gln Ile Glu Glu Lys
35 40 45

Glu Lys Lys Glu Lys Pro Lys Ser Asp Lys Thr Glu Glu Ile Ala Glu
50 55 60

Glu Glu Glu Thr Val Phe Pro Lys Ala Lys Gln Val Lys Lys Lys Ala

- 274 -

65				70						75					80
Glu	Pro	Ser	Glu	Val	Asp	Met	Asn	Ser	Pro	Lys	Ser	Lys	Lys	Ala	Lys
				85					90					95	
Lys	Lys	Glu	Glu	Pro	Ser	Gln	Asn	Asp	Ile	Ser	Pro	Lys	Thr	Lys	Ser
			100					105					110		
Leu	Arg	Lys	Lys	Lys	Glu	Pro	Ile	Glu	Lys	Lys	Val	Val	Ser	Ser	Lys
		115					120					125			
Thr	Lys	Lys	Val	Thr	Lys	Asn	Glu	Glu	Pro	Ser	Glu	Glu	Glu	Ile	Asp
	130					135					140				
Ala	Pro	Lys	Pro	Lys	Lys	Met	Lys	Lys	Glu	Lys	Glu	Met	Asn	Gly	Glu
145					150					155					160
Thr	Arg	Glu	Lys	Ser	Pro	Lys	Leu	Lys	Asn	Gly	Phe	Pro	His	Pro	Glu
				165					170					175	
Pro	Asp	Cys	Asn	Pro	Ser	Glu	Ala	Ala	Ser	Glu	Glu	Ser	Asn	Ser	Glu
			180					185					190		
Ile	Glu	Gln	Glu	Ile	Pro	Val	Glu	Gln	Lys	Glu	Gly	Ala	Phe	Ser	Asn
		195					200					205			
Phe	Pro	Ile	Ser	Glu	Glu	Thr	Ile	Lys	Leu	Leu	Lys	Gly	Arg	Gly	Val
	210					215					220				
Thr	Phe	Leu	Phe	Pro	Ile	Gln	Ala	Lys	Thr	Phe	His	His	Val	Tyr	Ser
225					230					235					240
Gly	Lys	Asp	Leu	Ile	Ala	Gln	Ala	Arg	Thr	Gly	Thr	Gly	Lys	Thr	Phe
				245					250					255	
Ser	Phe	Ala	Ile	Pro	Leu	Ile	Glu	Lys	Leu	His	Gly	Glu	Leu	Gln	Asp
			260					265					270		
Arg	Lys	Arg	Gly	Arg	Ala	Pro	Gln	Val	Leu	Val	Leu	Ala	Pro	Thr	Arg
		275					280					285			
Glu	Leu	Ala	Asn	Gln	Val	Ser	Lys	Asp	Phe	Ser	Asp	Ile	Thr	Lys	Lys
	290					295					300				

- 275 -

Leu Ser Val Ala Cys Phe Tyr Gly Gly Thr Pro Tyr Gly Gly Gln Phe
 305 310 315 320

Glu Arg Met Arg Asn Gly Ile Asp Ile Leu Val Gly Thr Pro Gly Arg
 325 330 335

Ile Lys Asp His Ile Gln Asn Gly Lys Leu Asp Leu Thr Lys Leu Lys
 340 345 350

His Val Val Leu Asp Glu Val Asp Gln Met Leu Asp Met Gly Phe Ala
 355 360 365

Asp Gln Val Glu Glu Ile Leu Ser Val Ala Tyr Lys Lys Asp Ser Glu
 370 375 380

Asp Asn Pro Gln Thr Leu Leu Phe Ser Ala Thr Cys Pro His Trp Val
 385 390 395 400

Phe Asn Val Ala Lys Lys Tyr Met Lys Ser Thr Tyr Glu Gln Val Asp
 405 410 415

Leu Ile Gly Lys Lys Thr Gln Lys Thr Ala Ile Thr Val Glu His Leu
 420 425 430

Ala Ile Lys Cys His Trp Thr Gln Arg Ala Ala Val Ile Gly Asp Val
 435 440 445

Ile Arg Val Tyr Ser Gly His Gln Gly Arg Thr Ile Ile Phe Cys Glu
 450 455 460

Thr Lys Lys Glu Ala Gln Glu Leu Ser Gln Asn Ser Ala Ile Lys Gln
 465 470 475 480

Asp Ala Gln Ser Leu His Gly Asp Ile Pro Gln Lys Gln Arg Glu Ile
 485 490 495

Thr Leu Lys Gly Phe Arg Asn Gly Ser Phe Gly Val Leu Val Ala Thr
 500 505 510

Asn Val Ala Ala Arg Gly Leu Asp Ile Pro Glu Val Asp Leu Val Ile
 515 520 525

Gln Ser Ser Pro Pro Lys Asp Val Glu Ser Tyr Ile His Arg Ser Gly
 530 535 540

- 276 -

Arg Thr Gly Arg Ala Gly Arg Thr Gly Val Cys Ile Cys Phe Tyr Gln
545 550 555 560

His Lys Glu Glu Tyr Gln Leu Val Gln Val Glu Gln Lys Ala Gly Ile
565 570 575

Lys Phe Lys Arg Ile Gly Val Pro Ser Ala Thr Glu Ile Ile Lys Ala
580 585 590

Ser Ser Lys Asp Ala Ile Arg Leu Leu Asp Ser Val Pro Pro Thr Ala
595 600 605

Ile Ser His Phe Lys Gln Ser Ala Glu Lys Leu Ile Glu Glu Lys Gly
610 615 620

Ala Val Glu Ala Leu Ala Ala Ala Leu Ala His Ile Ser Gly Ala Thr
625 630 635 640

Ser Val Asp Gln Arg Ser Leu Ile Asn Ser Asn Val Gly Phe Val Thr
645 650 655

Met Ile Leu Gln Cys Ser Ile Glu Met Pro Asn Ile Ser Tyr Ala Trp
660 665 670

Lys Glu Leu Lys Glu Gln Leu Gly Glu Glu Ile Asp Ser Lys Val Lys
675 680 685

Gly Met Val Phe Leu Lys Gly Lys Leu Gly Val Cys Phe Asp Val Pro
690 695 700

Thr Ala Ser Val Thr Glu Ile Gln Glu Lys Trp His Asp Ser Arg Arg
705 710 715 720

Trp Gln Leu Ser Val Ala Thr Glu Gln Pro Glu Leu Glu Gly Pro Arg
725 730 735

Glu Gly Tyr Gly Gly Phe Arg Gly Gln Arg Glu Gly Ser Arg Gly Phe
740 745 750

Arg Gly Gln Arg Asp Gly Asn Arg Arg Phe Arg Gly Gln Arg Glu Gly
755 760 765

Ser Arg Gly Pro Arg Gly Gln Arg Ser Gly Gly Gly Asn Lys Ser Asn
770 775 780

- 277 -

Arg Ser Gln Asn Lys Gly Gln Lys Arg Ser Phe Ser Lys Ala Phe Gly
 785 790 795 800

Gln

<210> 131

<211> 177

<212> PRT

<213> Homo sapiens

<400> 131

Asp Ile Phe Gln Lys Tyr Ser Asp Val Ile Ala Gly Gln Phe Tyr Gly
 1 5 10 15

His Thr His Arg Asp Ser Ile Met Val Leu Ser Asp Lys Lys Gly Ser
 20 25 30

Pro Val Asn Ser Leu Phe Val Ala Pro Ala Val Thr Pro Val Lys Ser
 35 40 45

Val Leu Glu Lys Gln Thr Asn Asn Pro Gly Ile Arg Leu Phe Gln Tyr
 50 55 60

Asp Pro Arg Asp Tyr Lys Leu Leu Asp Met Leu Gln Tyr Tyr Leu Asn
 65 70 75 80

Leu Thr Glu Ala Asn Leu Lys Gly Glu Ser Ile Trp Lys Leu Glu Tyr
 85 90 95

Ile Leu Thr Gln Thr Tyr Asp Ile Glu Asp Leu Gln Pro Glu Ser Leu
 100 105 110

Tyr Gly Leu Ala Lys Gln Phe Thr Ile Leu Asp Ser Lys Gln Phe Ile
 115 120 125

Lys Tyr Tyr Asn Tyr Phe Phe Val Ser Tyr Asp Ser Ser Val Thr Cys
 130 135 140

Asp Lys Thr Cys Lys Ala Phe Gln Ile Cys Ala Ile Met Asn Leu Asp

- 278 -

145 150 155 160

Asn Ile Ser Tyr Ala Asp Cys Leu Lys Gln Leu Tyr Ile Lys His Lys
165 170 175

Tyr

<210> 132

<211> 751

<212> PRT

<213> Homo sapiens

<400> 132

Met Ala Phe Arg Thr Ile Cys Val Leu Val Gly Val Phe Ile Cys Ser
1 5 10 15

Ile Cys Val Lys Gly Ser Ser Gln Pro Gln Ala Arg Val Tyr Leu Thr
20 25 30

Phe Asp Glu Leu Arg Glu Thr Lys Thr Ser Glu Tyr Phe Ser Leu Ser
35 40 45

His His Pro Leu Asp Tyr Arg Ile Leu Leu Met Asp Glu Asp Gln Asp
50 55 60

Arg Ile Tyr Val Gly Ser Lys Asp His Ile Leu Ser Leu Asn Ile Asn
65 70 75 80

Asn Ile Ser Gln Glu Ala Leu Ser Val Phe Trp Pro Ala Ser Thr Ile
85 90 95

Lys Val Glu Glu Cys Lys Met Ala Gly Lys Asp Pro Thr His Gly Cys
100 105 110

Gly Asn Phe Val Arg Val Ile Gln Thr Phe Asn Arg Thr His Leu Tyr
115 120 125

Val Cys Gly Ser Gly Ala Phe Ser Pro Val Cys Thr Tyr Leu Asn Arg
130 135 140

- 279 -

Gly	Arg	Arg	Ser	Glu	Asp	Gln	Val	Phe	Met	Ile	Asp	Ser	Lys	Cys	Glu	145	150	155	160
Ser	Gly	Lys	Gly	Arg	Cys	Ser	Phe	Asn	Pro	Asn	Val	Asn	Thr	Val	Ser	165	170	175	
Val	Met	Ile	Asn	Glu	Glu	Leu	Phe	Ser	Gly	Met	Tyr	Ile	Asp	Phe	Met	180	185	190	
Gly	Thr	Asp	Ala	Ala	Ile	Phe	Arg	Ser	Leu	Thr	Lys	Arg	Asn	Ala	Val	195	200	205	
Arg	Thr	Asp	Gln	His	Asn	Ser	Lys	Trp	Leu	Ser	Glu	Pro	Met	Phe	Val	210	215	220	
Asp	Ala	His	Val	Ile	Pro	Asp	Gly	Thr	Asp	Pro	Asn	Asp	Ala	Lys	Val	225	230	235	240
Tyr	Phe	Phe	Phe	Lys	Glu	Lys	Leu	Thr	Asp	Asn	Asn	Arg	Ser	Thr	Lys	245	250	255	
Gln	Ile	His	Ser	Met	Ile	Ala	Arg	Ile	Cys	Pro	Asn	Asp	Thr	Gly	Gly	260	265	270	
Leu	Arg	Ser	Leu	Val	Asn	Lys	Trp	Thr	Thr	Phe	Leu	Lys	Ala	Arg	Leu	275	280	285	
Val	Cys	Ser	Val	Thr	Asp	Glu	Asp	Gly	Pro	Glu	Thr	His	Phe	Asp	Glu	290	295	300	
Leu	Glu	Asp	Val	Phe	Leu	Leu	Glu	Thr	Asp	Asn	Pro	Arg	Thr	Thr	Leu	305	310	315	320
Val	Tyr	Gly	Ile	Phe	Thr	Thr	Ser	Ser	Ser	Val	Phe	Lys	Gly	Ser	Ala	325	330	335	
Val	Cys	Val	Tyr	His	Leu	Ser	Asp	Ile	Gln	Thr	Val	Phe	Asn	Gly	Pro	340	345	350	
Phe	Ala	His	Lys	Glu	Gly	Pro	Asn	His	Gln	Leu	Ile	Ser	Tyr	Gln	Gly	355	360	365	
Arg	Ile	Pro	Tyr	Pro	Arg	Pro	Gly	Thr	Cys	Pro	Gly	Gly	Ala	Phe	Thr	370	375	380	

- 280 -

Pro Asn Met Arg Thr Thr Lys Glu Phe Pro Asp Asp Val Val Thr Phe
385 390 395 400

Ile Arg Asn His Pro Leu Met Tyr Asn Ser Ile Tyr Pro Ile His Lys
405 410 415

Arg Pro Leu Ile Val Arg Ile Gly Thr Asp Tyr Lys Tyr Thr Lys Ile
420 425 430

Ala Val Asp Arg Val Asn Ala Ala Asp Gly Arg Tyr His Val Leu Phe
435 440 445

Leu Gly Thr Asp Arg Gly Thr Val Gln Lys Val Val Val Leu Pro Thr
450 455 460

Asn Asn Ser Val Ser Gly Glu Leu Ile Leu Glu Glu Leu Glu Val Phe
465 470 475 480

Lys Asn His Ala Pro Ile Thr Thr Met Lys Ile Ser Ser Lys Lys Gln
485 490 495

Gln Leu Tyr Val Ser Ser Asn Glu Gly Val Ser Gln Val Ser Leu His
500 505 510

Arg Cys His Ile Tyr Gly Thr Ala Cys Ala Asp Cys Cys Leu Ala Arg
515 520 525

Asp Pro Tyr Cys Ala Trp Asp Gly His Ser Cys Ser Arg Phe Tyr Pro
530 535 540

Thr Gly Lys Arg Arg Ser Arg Arg Gln Asp Val Arg His Gly Asn Pro
545 550 555 560

Leu Thr Gln Cys Arg Gly Phe Asn Leu Lys Ala Tyr Arg Asn Ala Ala
565 570 575

Glu Ile Val Gln Tyr Gly Val Lys Asn Asn Thr Thr Phe Leu Glu Cys
580 585 590

Ala Pro Lys Ser Pro Gln Ala Ser Ile Lys Trp Leu Leu Gln Lys Asp
595 600 605

Lys Asp Arg Arg Lys Glu Val Lys Leu Asn Glu Arg Ile Ile Ala Thr
610 615 620

- 281 -

Ser Gln Gly Leu Leu Ile Arg Ser Val Gln Gly Ser Asp Gln Gly Leu
625 630 635 640

Tyr His Cys Ile Ala Thr Glu Asn Ser Phe Lys Gln Thr Ile Ala Lys
645 650 655

Ile Asn Phe Lys Val Leu Asp Ser Glu Met Val Ala Val Val Thr Asp
660 665 670

Lys Trp Ser Pro Trp Thr Trp Ala Ser Ser Val Arg Ala Leu Pro Phe
675 680 685

His Pro Lys Asp Ile Met Gly Ala Phe Ser His Ser Glu Met Gln Met
690 695 700

Ile Asn Gln Tyr Cys Lys Asp Thr Arg Gln Gln His Gln Gln Gly Asp
705 710 715 720

Glu Ser Gln Lys Met Arg Gly Asp Tyr Gly Lys Leu Lys Ala Leu Ile
725 730 735

Asn Ser Arg Lys Ser Arg Asn Arg Arg Asn Gln Leu Pro Glu Ser
740 745 750

<210> 133

<211> 503

<212> PRT

<213> Homo sapiens

<400> 133

Met Glu Pro Ala Gly Pro Ala Pro Gly Arg Leu Gly Pro Leu Leu Cys
1 5 10 15

Leu Leu Leu Ala Ala Ser Cys Ala Trp Ser Gly Val Ala Gly Glu Glu
20 25 30

Glu Leu Gln Val Ile Gln Pro Asp Lys Ser Val Ser Val Ala Ala Gly
35 40 45

Glu Ser Ala Ile Leu His Cys Thr Val Thr Ser Leu Ile Pro Val Gly

- 282 -

50		55		60											
Pro 65	Ile	Gln	Trp	Phe	Arg 70	Gly	Ala	Gly	Pro	Ala 75	Arg	Glu	Leu	Ile	Tyr 80
Asn	Gln	Lys	Glu	Gly 85	His	Phe	Pro	Arg	Val 90	Thr	Thr	Val	Ser	Glu 95	Ser
Thr	Lys	Arg	Glu 100	Asn	Met	Asp	Phe	Ser 105	Ile	Ser	Ile	Ser	Asn 110	Ile	Thr
Pro	Ala	Asp 115	Ala	Gly	Thr	Tyr	Tyr 120	Cys	Val	Lys	Phe	Arg 125	Lys	Gly	Ser
Pro 130	Asp	Thr	Glu	Phe	Lys	Ser 135	Gly	Ala	Gly	Thr	Glu 140	Leu	Ser	Val	Arg
Ala 145	Lys	Pro	Ser	Ala	Pro 150	Val	Val	Ser	Gly	Pro 155	Ala	Ala	Arg	Ala	Thr 160
Pro	Gln	His	Thr	Val 165	Ser	Phe	Thr	Cys	Glu 170	Ser	His	Gly	Phe	Ser 175	Pro
Arg	Asp	Ile	Thr 180	Leu	Lys	Trp	Phe	Lys 185	Asn	Gly	Asn	Glu	Leu 190	Ser	Asp
Phe	Gln	Thr 195	Asn	Val	Asp	Pro	Val 200	Gly	Glu	Ser	Val	Ser 205	Tyr	Ser	Ile
His 210	Ser	Thr	Ala	Lys	Val 215	Val	Leu	Thr	Arg	Glu	Asp 220	Val	His	Ser	Gln
Val 225	Ile	Cys	Glu	Val	Ala 230	His	Val	Thr	Leu	Gln 235	Gly	Asp	Pro	Leu 240	Arg
Gly	Thr	Ala	Asn 245	Leu	Ser	Glu	Thr	Ile	Arg 250	Val	Pro	Pro	Thr	Leu 255	Glu
Val	Thr	Gln 260	Gln	Pro	Val	Arg	Ala	Glu 265	Asn	Gln	Val	Asn 270	Val	Thr	Cys
Gln 275	Val	Arg	Lys	Phe	Tyr	Pro	Gln 280	Arg	Leu	Gln	Leu	Thr 285	Trp	Leu	Glu

- 283 -

Asn Gly Asn Val Ser Arg Thr Glu Thr Ala Ser Thr Val Thr Glu Asn
290 295 300

Lys Asp Gly Thr Tyr Asn Trp Met Ser Trp Leu Leu Val Asn Val Ser
305 310 315 320

Ala His Arg Asp Asp Val Lys Leu Thr Cys Gln Val Glu His Asp Gly
325 330 335

Gln Pro Ala Val Ser Lys Ser His Asp Leu Lys Val Ser Ala His Pro
340 345 350

Lys Glu Gln Gly Ser Asn Thr Ala Ala Glu Asn Thr Gly Ser Asn Glu
355 360 365

Arg Asn Ile Tyr Ile Val Val Gly Val Val Cys Thr Leu Leu Val Ala
370 375 380

Leu Leu Met Ala Ala Leu Tyr Leu Val Arg Ile Arg Gln Lys Lys Ala
385 390 395 400

Gln Gly Ser Thr Ser Ser Thr Arg Leu His Glu Pro Glu Lys Asn Ala
405 410 415

Arg Glu Ile Thr Gln Asp Thr Asn Asp Ile Thr Tyr Ala Asp Leu Asn
420 425 430

Leu Pro Lys Gly Lys Lys Pro Ala Pro Gln Ala Ala Glu Pro Asn Asn
435 440 445

His Thr Glu Tyr Ala Ser Ile Gln Thr Ser Pro Gln Pro Ala Ser Glu
450 455 460

Asp Thr Leu Thr Tyr Ala Asp Leu Asp Met Val His Leu Asn Arg Thr
465 470 475 480

Pro Lys Gln Pro Ala Pro Lys Pro Glu Pro Ser Phe Ser Glu Tyr Ala
485 490 495

Ser Val Gln Val Pro Arg Lys
500

<210> 134

- 284 -

<211> 347

<212> PRT

<213> Homo sapiens

<400> 134

Met Ala Leu Leu Phe Ser Leu Ile Leu Ala Ile Cys Thr Arg Pro Gly
 1 5 10 15

Phe Leu Ala Ser Pro Ser Gly Val Arg Leu Val Gly Gly Leu His Arg
 20 25 30

Cys Glu Gly Arg Val Glu Val Glu Gln Lys Gly Gln Trp Gly Thr Val
 35 40 45

Cys Asp Asp Gly Trp Asp Ile Lys Asp Val Ala Val Leu Cys Arg Glu
 50 55 60

Leu Gly Cys Gly Ala Ala Ser Gly Thr Pro Ser Gly Ile Leu Tyr Glu
 65 70 75 80

Pro Pro Ala Glu Lys Glu Gln Lys Val Leu Ile Gln Ser Val Ser Cys
 85 90 95

Thr Gly Thr Glu Asp Thr Leu Ala Gln Cys Glu Gln Glu Glu Val Tyr
 100 105 110

Asp Cys Ser His Asp Glu Asp Ala Gly Ala Ser Cys Glu Asn Pro Glu
 115 120 125

Ser Ser Phe Ser Pro Val Pro Glu Gly Val Arg Leu Ala Asp Gly Pro
 130 135 140

Gly His Cys Lys Gly Arg Val Glu Val Lys His Gln Asn Gln Trp Tyr
 145 150 155 160

Thr Val Cys Gln Thr Gly Trp Ser Leu Arg Ala Ala Lys Val Val Cys
 165 170 175

Arg Gln Leu Gly Cys Gly Arg Ala Val Leu Thr Gln Lys Arg Cys Asn
 180 185 190

Lys His Ala Tyr Gly Arg Lys Pro Ile Trp Leu Ser Gln Met Ser Cys

- 285 -

195

200

205

Ser Gly Arg Glu Ala Thr Leu Gln Asp Cys Pro Ser Gly Pro Trp Gly
210 215 220

Lys Asn Thr Cys Asn His Asp Glu Asp Thr Trp Val Glu Cys Glu Asp
225 230 235 240

Pro Phe Asp Leu Arg Leu Val Gly Gly Asp Asn Leu Cys Ser Gly Arg
245 250 255

Leu Glu Val Leu His Lys Gly Val Trp Gly Ser Val Cys Asp Asp Asn
260 265 270

Trp Gly Glu Lys Glu Asp Gln Val Val Cys Lys Gln Leu Gly Cys Gly
275 280 285

Lys Ser Leu Ser Pro Ser Phe Arg Asp Arg Lys Cys Tyr Gly Pro Gly
290 295 300

Val Gly Arg Ile Trp Leu Asp Asn Val Arg Cys Ser Gly Glu Glu Gln
305 310 315 320

Ser Leu Glu Gln Cys Gln His Arg Phe Trp Gly Phe His Asp Cys Thr
325 330 335

His Gln Glu Asp Val Ala Val Ile Cys Ser Gly
340 345

<210> 135

<211> 277

<212> PRT

<213> Homo sapiens

<400> 135

Met Ala Ala Val Ser Val Tyr Ala Pro Pro Val Gly Gly Phe Ser Phe
1 5 10 15

Asp Asn Cys Arg Arg Asn Ala Val Leu Glu Ala Asp Phe Ala Lys Arg
20 25 30

- 286 -

Gly Tyr Lys Leu Pro Lys Val Arg Lys Thr Gly Thr Thr Ile Ala Gly
 35 40 45

Val Val Tyr Lys Asp Gly Ile Val Leu Gly Ala Asp Thr Arg Ala Thr
 50 55 60

Glu Gly Met Val Val Ala Asp Lys Asn Cys Ser Lys Ile His Phe Ile
 65 70 75 80

Ser Pro Asn Ile Tyr Cys Cys Gly Ala Gly Thr Ala Ala Asp Thr Asp
 85 90 95

Met Thr Thr Gln Leu Ile Ser Ser Asn Leu Glu Leu His Ser Leu Ser
 100 105 110

Thr Gly Arg Leu Pro Arg Val Val Thr Ala Asn Arg Met Leu Lys Gln
 115 120 125

Met Leu Phe Arg Tyr Gln Gly Tyr Ile Gly Ala Ala Leu Val Leu Gly
 130 135 140

Gly Val Asp Val Thr Gly Pro His Leu Tyr Ser Ile Tyr Pro His Gly
 145 150 155 160

Ser Thr Asp Lys Leu Pro Tyr Val Thr Met Gly Ser Gly Ser Leu Ala
 165 170 175

Ala Met Ala Val Phe Glu Asp Lys Phe Arg Pro Asp Met Glu Glu Glu
 180 185 190

Glu Ala Lys Asn Leu Val Ser Glu Ala Ile Ala Ala Gly Ile Phe Asn
 195 200 205

Asp Leu Gly Ser Gly Ser Asn Ile Asp Leu Cys Val Ile Ser Lys Asn
 210 215 220

Lys Leu Asp Phe Leu Arg Pro Tyr Thr Val Pro Asn Lys Lys Gly Thr
 225 230 235 240

Arg Leu Gly Arg Tyr Arg Cys Glu Lys Gly Thr Thr Ala Val Leu Thr
 245 250 255

Glu Lys Ile Thr Pro Leu Glu Ile Glu Val Leu Glu Glu Thr Val Gln
 260 265 270

- 287 -

Thr Met Asp Thr Ser
275

<210> 136

<211> 763

<212> PRT

<213> Homo sapiens

<400> 136

Met Ala Ala Thr Gly Thr Ala Ala Ala Ala Ala Thr Gly Arg Leu Leu
1 5 10 15

Leu Leu Leu Leu Val Gly Leu Thr Ala Pro Ala Leu Ala Leu Ala Gly
20 25 30

Tyr Ile Glu Ala Leu Ala Ala Asn Ala Gly Thr Gly Phe Ala Val Ala
35 40 45

Glu Pro Gln Ile Ala Met Phe Cys Gly Lys Leu Asn Met His Val Asn
50 55 60

Ile Gln Thr Gly Lys Trp Glu Pro Asp Pro Thr Gly Thr Lys Ser Cys
65 70 75 80

Phe Glu Thr Lys Glu Glu Val Leu Gln Tyr Cys Gln Glu Met Tyr Pro
85 90 95

Glu Leu Gln Ile Thr Asn Val Met Glu Ala Asn Gln Arg Val Ser Ile
100 105 110

Asp Asn Trp Cys Arg Arg Asp Lys Lys Gln Cys Lys Ser Arg Phe Val
115 120 125

Thr Pro Phe Lys Cys Leu Val Gly Glu Phe Val Ser Asp Val Leu Leu
130 135 140

Val Pro Glu Lys Cys Gln Phe Phe His Lys Glu Arg Met Glu Val Cys
145 150 155 160

Glu Asn His Gln His Trp His Thr Val Val Lys Glu Ala Cys Leu Thr
165 170 175

- 288 -

Gln Gly Met Thr Leu Tyr Ser Tyr Gly Met Leu Leu Pro Cys Gly Val
 180 185 190

Asp Gln Phe His Gly Thr Glu Tyr Val Cys Cys Pro Gln Thr Lys Ile
 195 200 205

Ile Gly Ser Val Ser Lys Glu Glu Glu Glu Glu Asp Glu Glu Glu Glu
 210 215 220

Glu Glu Glu Asp Glu Glu Glu Asp Tyr Asp Val Tyr Lys Ser Glu Phe
 225 230 235 240

Pro Thr Glu Ala Asp Leu Glu Asp Phe Thr Glu Ala Ala Val Asp Glu
 245 250 255

Asp Asp Glu Asp Glu Glu Glu Gly Glu Glu Val Val Glu Asp Arg Asp
 260 265 270

Tyr Tyr Tyr Asp Thr Phe Lys Gly Asp Asp Tyr Asn Glu Glu Asn Pro
 275 280 285

Thr Glu Pro Gly Ser Asp Gly Thr Met Ser Asp Lys Glu Ile Thr His
 290 295 300

Asp Val Lys Ala Val Cys Ser Gln Glu Ala Met Thr Gly Pro Cys Arg
 305 310 315 320

Ala Val Met Pro Arg Trp Tyr Phe Asp Leu Ser Lys Gly Lys Cys Val
 325 330 335

Arg Phe Ile Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Glu Ser
 340 345 350

Glu Asp Tyr Cys Met Ala Val Cys Lys Ala Met Ile Pro Pro Thr Pro
 355 360 365

Leu Pro Thr Asn Asp Val Asp Val Tyr Phe Glu Thr Ser Ala Asp Asp
 370 375 380

Asn Glu His Ala Arg Phe Gln Lys Ala Lys Glu Gln Leu Glu Ile Arg
 385 390 395 400

His Arg Asn Arg Met Asp Arg Val Lys Lys Glu Trp Glu Glu Ala Glu

- 289 -

405					410					415					
Leu	Gln	Ala	Lys	Asn	Leu	Pro	Lys	Ala	Glu	Arg	Gln	Thr	Leu	Ile	Gln
			420					425					430		
His	Phe	Gln	Ala	Met	Val	Lys	Ala	Leu	Glu	Lys	Glu	Ala	Ala	Ser	Glu
		435					440					445			
Lys	Gln	Gln	Leu	Val	Glu	Thr	His	Leu	Ala	Arg	Val	Glu	Ala	Met	Leu
	450					455					460				
Asn	Asp	Arg	Arg	Arg	Met	Ala	Leu	Glu	Asn	Tyr	Leu	Ala	Ala	Leu	Gln
465						470				475					480
Ser	Asp	Pro	Pro	Arg	Pro	His	Arg	Ile	Leu	Gln	Ala	Leu	Arg	Arg	Tyr
				485					490					495	
Val	Arg	Ala	Glu	Asn	Lys	Asp	Arg	Leu	His	Thr	Ile	Arg	His	Tyr	Gln
			500					505					510		
His	Val	Leu	Ala	Val	Asp	Pro	Glu	Lys	Ala	Ala	Gln	Met	Lys	Ser	Gln
		515					520					525			
Val	Met	Thr	His	Leu	His	Val	Ile	Glu	Glu	Arg	Arg	Asn	Gln	Ser	Leu
	530					535					540				
Ser	Leu	Leu	Tyr	Lys	Val	Pro	Tyr	Val	Ala	Gln	Glu	Ile	Gln	Glu	Glu
545						550				555					560
Ile	Asp	Glu	Leu	Leu	Gln	Glu	Gln	Arg	Ala	Asp	Met	Asp	Gln	Phe	Thr
				565					570					575	
Ala	Ser	Ile	Ser	Glu	Thr	Pro	Val	Asp	Val	Arg	Val	Ser	Ser	Glu	Glu
			580					585					590		
Ser	Glu	Glu	Ile	Pro	Pro	Phe	His	Pro	Phe	His	Pro	Phe	Pro	Ala	Leu
		595					600					605			
Pro	Glu	Asn	Glu	Asp	Thr	Gln	Pro	Glu	Leu	Tyr	His	Pro	Met	Lys	Lys
	610					615					620				
Gly	Ser	Gly	Val	Gly	Glu	Gln	Asp	Gly	Gly	Leu	Ile	Gly	Ala	Glu	Glu
625						630				635					640

- 290 -

Lys Val Ile Asn Ser Lys Asn Lys Val Asp Glu Asn Met Val Ile Asp
645 650 655

Glu Thr Leu Asp Val Lys Glu Met Ile Phe Asn Ala Glu Arg Val Gly
660 665 670

Gly Leu Glu Glu Glu Arg Glu Ser Val Gly Pro Leu Arg Glu Asp Phe
675 680 685

Ser Leu Ser Ser Ser Ala Leu Ile Gly Leu Leu Val Ile Ala Val Ala
690 695 700

Ile Ala Thr Val Ile Val Ile Ser Leu Val Met Leu Arg Lys Arg Gln
705 710 715 720

Tyr Gly Thr Ile Ser His Gly Ile Val Glu Val Asp Pro Met Leu Thr
725 730 735

Pro Glu Glu Arg His Leu Asn Lys Met Gln Asn His Gly Tyr Glu Asn
740 745 750

Pro Thr Tyr Lys Tyr Leu Glu Gln Met Gln Ile
755 760

<210> 137

<211> 251

<212> PRT

<213> Homo sapiens

<400> 137

Met Lys Ile Ser Phe Ile Glu Pro Ala Ile Leu Leu Asn Ala Phe Ala
1 5 10 15

Met Thr Leu Thr Ile Pro Leu Thr Ala Gln Tyr Val Tyr Arg Arg Ile
20 25 30

Trp Glu Glu Thr Gly Asn Tyr Thr Phe Ala Ser Asn Gly Ser Glu Cys
35 40 45

Asp Gln Asn Lys Ser Ser Ser Ile Phe Ala Phe Arg Glu Glu Val Gln
50 55 60

- 291 -

Lys Lys Ala Ser Leu Phe Asn Leu Gln Val Glu Met Ser Ala Leu Ile
65 70 75 80

Pro Gly Leu Val Ser Thr Phe Met Leu Leu Ala Ser Ser Asp Asn His
85 90 95

Gly Arg Lys Leu Pro Met Val Leu Ser Ser Leu Gly Ser Leu Gly Thr
100 105 110

Asn Thr Trp Leu Cys Met Met Ser Tyr Phe Asp Leu Pro Leu Gln Leu
115 120 125

Leu Ile Ala Ser Thr Phe Ile Gly Ala Leu Phe Gly Asn Tyr Thr Thr
130 135 140

Phe Trp Gly Ala Cys Phe Ala Tyr Ile Val Asp Gln Gln Lys Glu Tyr
145 150 155 160

Lys His Arg Ile Ile Arg Ile Ala Ile Leu Asp Phe Met Leu Gly Val
165 170 175

Val Thr Gly Leu Thr Gly Leu Ser Ser Gly Tyr Phe Ile Arg Glu Leu
180 185 190

Gly Phe Val Trp Ser Tyr Phe Ile Thr Ala Met Val Leu Ile Val Asn
195 200 205

Leu Ala Tyr Ile Leu Phe Phe Leu Asn Asp Pro Ile Lys Glu Ser Ser
210 215 220

Ser Gln Ile Val Thr Met Ser Cys Ile Glu Ser Leu Lys Asp Leu Phe
225 230 235 240

Tyr Arg Thr Tyr Met Leu Phe Lys Asn Gly Ser
245 250

<210> 138

<211> 283

<212> PRT

<213> Homo sapiens

- 292 -

<400> 138

Met Ala Val Pro Pro Thr Tyr Ala Asp Leu Gly Lys Ser Ala Arg Asp
 1 5 10 15

Val Phe Thr Lys Gly Tyr Gly Phe Gly Leu Ile Lys Leu Asp Leu Lys
 20 25 30

Thr Lys Ser Glu Asn Gly Leu Glu Phe Thr Ser Ser Gly Ser Ala Asn
 35 40 45

Thr Glu Thr Thr Lys Val Thr Gly Ser Leu Glu Thr Lys Tyr Arg Trp
 50 55 60

Thr Glu Tyr Gly Leu Thr Phe Thr Glu Lys Trp Asn Thr Asp Asn Thr
 65 70 75 80

Leu Gly Thr Glu Ile Thr Val Glu Asp Gln Leu Ala Arg Gly Leu Lys
 85 90 95

Leu Thr Phe Asp Ser Ser Phe Ser Pro Asn Thr Gly Lys Lys Asn Ala
 100 105 110

Lys Ile Lys Thr Gly Tyr Lys Arg Glu His Ile Asn Leu Gly Cys Asp
 115 120 125

Met Asp Phe Asp Ile Ala Gly Pro Ser Ile Arg Gly Ala Leu Val Leu
 130 135 140

Gly Tyr Glu Gly Trp Leu Ala Gly Tyr Gln Met Asn Phe Glu Thr Ala
 145 150 155 160

Lys Ser Arg Val Thr Gln Ser Asn Phe Ala Val Gly Tyr Lys Thr Asp
 165 170 175

Glu Phe Gln Leu His Thr Asn Val Asn Asp Gly Thr Glu Phe Gly Gly
 180 185 190

Ser Ile Tyr Gln Lys Val Asn Lys Lys Leu Glu Thr Ala Val Asn Leu
 195 200 205

Ala Trp Thr Ala Gly Asn Ser Asn Thr Arg Phe Gly Ile Ala Ala Lys
 210 215 220

Tyr Gln Ile Asp Pro Asp Ala Cys Phe Ser Ala Lys Val Asn Asn Ser

225					230					235					240
Ser	Leu	Ile	Gly	Leu	Gly	Tyr	Thr	Gln	Thr	Leu	Lys	Pro	Gly	Ile	Lys
				245					250					255	
Leu	Thr	Leu	Ser	Ala	Leu	Leu	Asp	Gly	Lys	Asn	Val	Asn	Ala	Gly	Gly
			260					265					270		
His	Lys	Leu	Gly	Leu	Gly	Leu	Glu	Phe	Gln	Ala					
		275					280								

<400> 139

BNSDOCID: <WO 03031650A2 I >

- 294 -

Tyr Leu Gly Gln Phe Pro Asp Ile Lys Ser Arg Ile Ala Lys Arg Gly
 130 135 140

Arg Lys Leu Val Asp Tyr Asp Ser Ala Arg His His Tyr Glu Ser Leu
 145 150 155 160

Gln Thr Ala Lys Lys Lys Asp Glu Ala Lys Ile Ala Lys Ala Glu Glu
 165 170 175

Glu Leu Ile Lys Ala Gln Lys Val Phe Glu Glu Met Asn Val Asp Leu
 180 185 190

Gln Glu Glu Leu Pro Ser Leu Trp Asn Ser Arg Val Gly Phe Tyr Val
 195 200 205

Asn Thr Phe Gln Ser Ile Ala Gly Leu Glu Glu Asn Phe His Lys Glu
 210 215 220

Met Ser Lys Leu Asn Gln Asn Leu Asn Asp Val Leu Val Gly Leu Glu
 225 230 235 240

Lys Gln His Gly Ser Asn Thr Phe Thr Val Lys Ala Gln Pro Ser Asp
 245 250 255

Asn Ala Pro Ala Lys Gly Asn Lys Ser Pro Ser Pro Pro Asp Gly Ser
 260 265 270

Pro Ala Ala Thr Pro Glu Ile Arg Val Asn His Glu Pro Glu Pro Ala
 275 280 285

Gly Gly Ala Thr Pro Gly Ala Thr Leu Pro Lys Ser Pro Ser Gln Leu
 290 295 300

Arg Lys Gly Pro Pro Val Pro Pro Pro Pro Lys His Thr Pro Ser Lys
 305 310 315 320

Glu Val Lys Gln Glu Gln Ile Leu Ser Leu Phe Glu Asp Thr Phe Val
 325 330 335

Pro Glu Ile Ser Val Thr Thr Pro Ser Gln Pro Ala Glu Ala Ser Glu
 340 345 350

Val Ala Gly Gly Thr Gln Pro Ala Ala Gly Ala Gln Glu Pro Gly Glu
 355 360 365

-295 -

Thr Ala Ala Ser Glu Ala Ala Ser Ser Ser Leu Pro Ala Val Val Val
370 375 380

Glu Thr Phe Pro Ala Thr Val Asn Gly Thr Val Glu Gly Gly Ser Gly
385 390 395 400

Ala Gly Arg Leu Asp Leu Pro Pro Gly Phe Met Phe Lys Val Gln Ala
405 410 415

Gln His Asp Tyr Thr Ala Thr Asp Thr Asp Glu Leu Gln Leu Lys Ala
420 425 430

Gly Asp Val Val Leu Val Ile Pro Phe Gln Asn Pro Glu Glu Gln Asp
435 440 445

Glu Gly Trp Leu Met Gly Val Lys Glu Ser Asp Trp Asn Gln His Lys
450 455 460

Glu Leu Glu Lys Cys Arg Gly Val Phe Pro Glu Asn Phe Thr Glu Arg
465 470 475 480

Val Pro

<210> 140

<211> 1053

<212> PRT

<213> Homo sapiens

<400> 140

Met Ser Ser Glu Glu Ser Tyr Arg Ala Ile Leu Arg Tyr Leu Thr Asn
1 5 10 15

Glu Arg Glu Pro Tyr Ala Pro Gly Thr Glu Gly Asn Val Lys Arg Lys
20 25 30

Ile Arg Lys Ala Ala Ala Cys Tyr Val Val Arg Gly Gly Thr Leu Tyr
35 40 45

Tyr Gln Arg Arg Gln Arg His Arg Lys Thr Phe Ala Glu Leu Glu Val
50 55 60

- 296 -

Val Leu Gln Pro Glu Arg Arg Arg Asp Leu Ile Glu Ala Ala His Leu
65 70 75 80

Gly Pro Gly Gly Thr His His Thr Arg His Gln Thr Trp His Tyr Leu
85 90 95

Ser Lys Thr Tyr Trp Trp Arg Gly Ile Leu Lys Gln Val Lys Asp Tyr
100 105 110

Ile Lys Gln Cys Ser Lys Cys Gln Glu Lys Leu Asp Arg Ser Arg Pro
115 120 125

Ile Ser Asp Val Ser Glu Met Leu Glu Glu Leu Gly Leu Asp Leu Glu
130 135 140

Ser Gly Glu Glu Ser Asn Glu Ser Glu Asp Asp Leu Ser Asn Phe Thr
145 150 155 160

Ser Ser Pro Thr Thr Ala Ser Lys Pro Ala Lys Lys Lys Pro Val Ser
165 170 175

Lys His Glu Leu Val Phe Val Asp Thr Lys Gly Val Val Lys Arg Ser
180 185 190

Ser Pro Lys His Cys Gln Ala Val Leu Lys Gln Leu Asn Glu Gln Arg
195 200 205

Leu Ser Asn Gln Phe Cys Asp Val Thr Leu Leu Ile Glu Gly Glu Glu
210 215 220

Tyr Lys Ala His Lys Ser Val Leu Ser Ala Asn Ser Glu Tyr Phe Arg
225 230 235 240

Asp Leu Phe Ile Glu Lys Gly Ala Val Ser Ser His Glu Ala Val Val
245 250 255

Asp Leu Ser Gly Phe Cys Lys Ala Ser Phe Leu Pro Leu Leu Glu Phe
260 265 270

Ala Tyr Thr Ser Val Leu Ser Phe Asp Phe Cys Ser Met Ala Asp Val
275 280 285

Ala Ile Leu Ala Arg His Leu Phe Met Ser Glu Val Leu Glu Ile Cys

- 297 -

290	295	300
Glu Ser Val His Lys Leu Met Glu Glu Lys Gln Leu Thr Val Tyr Lys 305 310 315 320		
Lys Gly Glu Val Gln Thr Val Ala Ser Thr Gln Asp Leu Arg Val Gln 325 330 335		
Asn Gly Gly Thr Ala Pro Pro Val Ala Ser Ser Glu Gly Thr Thr Thr 340 345 350		
Ser Leu Pro Thr Glu Leu Gly Asp Cys Glu Ile Val Leu Leu Val Asn 355 360 365		
Gly Glu Leu Pro Glu Ala Glu Gln Asn Gly Glu Val Gly Arg Gln Pro 370 375 380		
Glu Pro Gln Val Ser Ser Glu Ala Glu Ser Ala Leu Ser Ser Val Gly 385 390 395 400		
Cys Ile Ala Asp Ser His Pro Glu Met Glu Ser Val Asp Leu Ile Thr 405 410 415		
Lys Asn Asn Gln Thr Glu Leu Glu Thr Ser Asn Asn Arg Glu Asn Asn 420 425 430		
Thr Val Ser Asn Ile His Pro Lys Leu Ser Lys Glu Asn Val Ile Ser 435 440 445		
Ser Ser Pro Glu Asp Ser Gly Met Gly Asn Asp Ile Ser Ala Glu Asp 450 455 460		
Ile Cys Ala Glu Asp Ile Pro Lys His Arg Gln Lys Val Asp Gln Pro 465 470 475 480		
Leu Lys Asp Gln Glu Asn Leu Val Ala Ser Thr Ala Lys Thr Asn Phe 485 490 495		
Gly Pro Asp Asp Asp Thr Tyr Arg Ser Arg Leu Arg Gln Arg Ser Val 500 505 510		
Asn Glu Gly Ala Tyr Ile Arg Leu His Lys Gly Met Glu Lys Lys Leu 515 520 525		

- 298 -

Gln Lys Arg Lys Ala Val Pro Lys Ser Ala Val Gln Gln Val Ala Gln
530 535 540

Lys Leu Val Gln Arg Gly Lys Lys Met Lys Gln Pro Lys Arg Asp Ala
545 550 555 560

Lys Glu Asn Thr Glu Glu Ala Ser His Lys Cys Gly Glu Cys Gly Met
565 570 575

Val Phe Gln Arg Arg Tyr Ala Leu Ile Met His Lys Leu Lys His Glu
580 585 590

Arg Ala Arg Asp Tyr Lys Cys Pro Leu Cys Lys Lys Gln Phe Gln Tyr
595 600 605

Ser Ala Ser Leu Arg Ala His Leu Ile Arg His Thr Arg Lys Asp Ala
610 615 620

Pro Ser Ser Ser Ser Ser Asn Ser Thr Ser Asn Glu Ala Ser Gly Thr
625 630 635 640

Ser Ser Glu Lys Gly Arg Thr Lys Arg Glu Phe Ile Cys Ser Ile Cys
645 650 655

Gly Arg Thr Leu Pro Lys Leu Tyr Ser Leu Arg Ile His Met Leu Lys
660 665 670

His Thr Gly Val Lys Pro His Ala Cys Gln Val Cys Gly Lys Thr Phe
675 680 685

Ile Tyr Lys His Gly Leu Lys Leu His Gln Ser Leu His Gln Ser Gln
690 695 700

Lys Gln Phe Gln Cys Glu Leu Cys Val Lys Ser Phe Val Thr Lys Arg
705 710 715 720

Ser Leu Gln Glu His Met Ser Ile His Thr Gly Glu Ser Lys Tyr Leu
725 730 735

Cys Ser Val Cys Gly Lys Ser Phe His Arg Gly Ser Gly Leu Ser Lys
740 745 750

His Phe Lys Lys His Gln Pro Lys Pro Glu Val Arg Gly Tyr His Cys
755 760 765

- 299 -

Thr Gln Cys Glu Lys Ser Phe Phe Glu Ala Arg Asp Leu Arg Gln His
 770 775 780

Met Asn Lys His Leu Gly Val Lys Pro Phe Gln Cys Gln Phe Cys Asp
 785 790 795 800

Lys Cys Tyr Ser Trp Lys Lys Asp Trp Tyr Ser His Val Lys Ser His
 805 810 815

Ser Val Thr Glu Pro Tyr Arg Cys Asn Ile Cys Gly Lys Glu Phe Tyr
 820 825 830

Glu Lys Ala Leu Phe Arg Arg His Val Lys Lys Ala Thr His Gly Lys
 835 840 845

Lys Gly Arg Ala Lys Gln Asn Leu Glu Arg Val Cys Glu Lys Cys Gly
 850 855 860

Arg Lys Phe Thr Gln Leu Arg Glu Tyr Arg Arg His Met Asn Asn His
 865 870 875 880

Glu Gly Val Lys Pro Phe Glu Cys Leu Thr Cys Gly Val Ala Trp Ala
 885 890 895

Asp Ala Arg Ser Leu Lys Arg His Val Arg Thr His Thr Gly Glu Arg
 900 905 910

Pro Tyr Val Cys Pro Val Cys Ser Glu Ala Tyr Ile Asp Ala Arg Thr
 915 920 925

Leu Arg Lys His Met Thr Lys Phe His Arg Asp Tyr Val Pro Cys Lys
 930 935 940

Ile Met Leu Glu Lys Asp Thr Leu Gln Phe His Asn Gln Gly Thr Gln
 945 950 955 960

Val Ala His Ala Val Ser Ile Leu Thr Ala Gly Met Gln Glu Gln Glu
 965 970 975

Ser Ser Gly Pro Gln Glu Leu Glu Thr Val Val Val Thr Gly Glu Thr
 980 985 990

Met Glu Ala Leu Glu Ala Val Ala Ala Thr Glu Glu Tyr Pro Ser Val
 995 1000 1005

- 300 -

Ser Thr Leu Ser Asp Gln Ser Ile Met Gln Val Val Asn Tyr Val
 1010 1015 1020

Leu Ala Gln Gln Gln Gly Gln Lys Leu Ser Glu Val Ala Glu Ala
 1025 1030 1035

Ile Gln Thr Val Lys Val Glu Val Ala His Ile Ser Gly Gly Glu
 1040 1045 1050

<210> 141

<211> 143

<212> PRT

<213> Homo sapiens

<400> 141

Met Ser Gln Thr Arg Asp Leu Gln Gly Gly Lys Ala Phe Gly Leu Leu
 1 5 10 15

Lys Ala Gln Gln Glu Glu Arg Leu Asp Glu Ile Asn Lys Gln Phe Leu
 20 25 30

His Asp Pro Lys Tyr Ser Ser Asp Glu Asp Leu Pro Ser Lys Leu Glu
 35 40 45

Gly Phe Lys Glu Lys Tyr Met Glu Phe Asp Leu Asn Gly Asn Gly Asp
 50 55 60

Ile Asp Ile Met Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro
 65 70 75 80

Lys Thr His Leu Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly
 85 90 95

Ser Gly Glu Thr Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly
 100 105 110

Lys Arg Ser Ala Ile Leu Lys Met Ile Leu Met Tyr Glu Glu Lys Ala
 115 120 125

Arg Glu Arg Lys Thr Asn Thr Pro Pro Ser Gln Glu Ser Pro Ile

- 301 -

130 135 140

<210> 142

<211> 178

<212> PRT

<213> Homo sapiens

<400> 142

Met His Val Asn Gly Lys Val Ala Leu Val Thr Gly Ala Ala Gln Gly
1 5 10 15

Ile Gly Arg Ala Phe Ala Glu Ala Leu Leu Leu Lys Gly Ala Lys Val
 20 25 30

Ala Leu Val Asp Trp Asn Leu Glu Ala Gly Val Gln Cys Lys Ala Ala
 35 40 45

Leu Asp Glu Gln Phe Glu Pro Gln Lys Thr Leu Phe Ile Gln Cys Asp
50 55 60

Val Ala Asp Gln Gln Gln Leu Arg Asp Thr Phe Arg Lys Val Val Asp
65 70 75 80

His Phe Gly Arg Leu Asp Ile Leu Val Asn Asn Ala Gly Val Asn Asn
 85 90 95

Lys Lys Asn Trp Glu Lys Thr Leu Gln Ile Asn Leu Val Ser Val Ile
 100 105 110

Ser Gly Thr Tyr Leu Gly Leu Asp Tyr Met Ser Lys Gln Asn Gly Gly
 115 120 125

Glu Gly Gly Ile Ile Ile Asn Met Ser Ser Leu Ala Gly Leu Met Pro
130 135 140

Val Ala Gln Gln Pro Val Tyr Cys Ala Ser Lys His Gly Ile Val Gly
145 150 155 160

Phe Thr Arg Ser Ala Ala Pro Thr Ile Asp Cys Gln Trp Ile Asp Asn
 165 170 175

- 302 -

Thr His

<210> 143

<211> 687

<212> PRT

<213> Homo sapiens

<400> 143

Met Ala Glu Glu Leu Val Leu Glu Arg Cys Asp Leu Glu Leu Glu Thr
 1 5 10 15

Asn Gly Arg Asp His His Thr Ala Asp Leu Cys Arg Glu Lys Leu Val
 20 25 30

Val Arg Arg Gly Gln Pro Phe Trp Leu Thr Leu His Phe Glu Gly Arg
 35 40 45

Asn Tyr Gln Ala Ser Val Asp Ser Leu Thr Phe Ser Val Val Thr Gly
 50 55 60

Pro Ala Pro Ser Gln Glu Ala Gly Thr Lys Ala Arg Phe Pro Leu Arg
 65 70 75 80

Asp Ala Val Glu Glu Gly Asp Trp Thr Ala Thr Val Val Asp Gln Gln
 85 90 95

Asp Cys Thr Leu Ser Leu Gln Leu Thr Thr Pro Ala Asn Ala Pro Ile
 100 105 110

Gly Leu Tyr Arg Leu Ser Leu Glu Ala Ser Thr Gly Tyr Gln Gly Ser
 115 120 125

Ser Phe Val Leu Gly His Phe Ile Leu Leu Phe Asn Ala Trp Cys Pro
 130 135 140

Ala Asp Ala Val Tyr Leu Asp Ser Glu Glu Glu Arg Gln Glu Tyr Val
 145 150 155 160

Leu Thr Gln Gln Gly Phe Ile Tyr Gln Gly Ser Ala Lys Phe Ile Lys
 165 170 175

- 303 -

Asn Ile Pro Trp Asn Phe Gly Gln Phe Gln Asp Gly Ile Leu Asp Ile
 180 185 190

Cys Leu Ile Leu Leu Asp Val Asn Pro Lys Phe Leu Lys Asn Ala Gly
 195 200 205

Arg Asp Cys Ser Arg Arg Ser Ser Pro Val Tyr Val Gly Arg Val Gly
 210 215 220

Ser Gly Met Val Asn Cys Asn Asp Asp Gln Gly Val Leu Leu Gly Arg
 225 230 235 240

Trp Asp Asn Asn Tyr Gly Asp Gly Val Ser Pro Met Ser Trp Ile Gly
 245 250 255

Ser Val Asp Ile Leu Arg Arg Trp Lys Asn His Gly Cys Gln Arg Val
 260 265 270

Lys Tyr Gly Gln Cys Trp Val Phe Ala Ala Val Ala Cys Thr Val Leu
 275 280 285

Arg Cys Leu Gly Ile Pro Thr Arg Val Val Thr Asn Tyr Asn Ser Ala
 290 295 300

His Asp Gln Asn Ser Asn Leu Leu Ile Glu Tyr Phe Arg Asn Glu Phe
 305 310 315 320

Gly Glu Ile Gln Gly Asp Lys Ser Glu Met Ile Trp Asn Phe His Cys
 325 330 335

Trp Val Glu Ser Trp Met Thr Arg Pro Asp Leu Gln Pro Gly Tyr Glu
 340 345 350

Gly Trp Gln Ala Leu Asp Pro Thr Pro Gln Glu Lys Ser Glu Gly Thr
 355 360 365

Tyr Cys Cys Gly Pro Val Pro Val Arg Ala Ile Lys Glu Gly Asp Leu
 370 375 380

Ser Thr Lys Tyr Asp Ala Pro Phe Val Phe Ala Glu Val Asn Ala Asp
 385 390 395 400

Val Val Asp Trp Ile Gln Gln Asp Asp Gly Ser Val His Lys Ser Ile
 405 410 415

- 304 -

Asn Arg Ser Leu Ile Val Gly Leu Lys Ile Ser Thr Lys Ser Val Gly
 420 425 430

Arg Asp Glu Arg Glu Asp Ile Thr His Thr Tyr Lys Tyr Pro Glu Gly
 435 440 445

Ser Ser Glu Glu Arg Glu Ala Phe Thr Arg Ala Asn His Leu Asn Lys
 450 455 460

Leu Ala Glu Lys Glu Glu Thr Gly Met Ala Met Arg Ile Arg Val Gly
 465 470 475 480

Gln Ser Met Asn Met Gly Ser Asp Phe Asp Val Phe Ala His Ile Thr
 485 490 495

Asn Asn Thr Ala Glu Glu Tyr Val Cys Arg Leu Leu Leu Cys Ala Arg
 500 505 510

Thr Val Ser Tyr Asn Gly Ile Leu Gly Pro Glu Cys Gly Thr Lys Tyr
 515 520 525

Leu Leu Asn Leu Thr Leu Glu Pro Phe Ser Glu Lys Ser Val Pro Leu
 530 535 540

Cys Ile Leu Tyr Glu Lys Tyr Arg Asp Cys Leu Thr Glu Ser Asn Leu
 545 550 555 560

Ile Lys Val Arg Ala Leu Leu Val Glu Pro Val Ile Asn Ser Tyr Leu
 565 570 575

Leu Ala Glu Arg Asp Leu Tyr Leu Glu Asn Pro Glu Ile Lys Ile Arg
 580 585 590

Ile Leu Gly Glu Pro Lys Gln Lys Arg Lys Leu Val Ala Glu Val Ser
 595 600 605

Leu Gln Asn Pro Leu Pro Val Ala Leu Glu Gly Cys Thr Phe Thr Val
 610 615 620

Glu Gly Ala Gly Leu Thr Glu Glu Gln Lys Thr Val Glu Ile Pro Asp
 625 630 635 640

Pro Val Glu Ala Gly Glu Glu Val Lys Val Arg Met Asp Leu Val Pro

- 305 -

645

650

655

Leu His Met Gly Leu His Lys Leu Val Val Asn Phe Glu Ser Asp Lys
 660 665 670

Leu Lys Ala Val Lys Gly Phe Arg Asn Val Ile Ile Gly Pro Ala
 675 680 685

<210> 144

<211> 277

<212> PRT

<213> Homo sapiens

<400> 144

Met Ala Ala Val Ser Val Tyr Ala Pro Pro Val Gly Gly Phe Ser Phe
 1 5 10 15

Asp Asn Cys Arg Arg Asn Ala Val Leu Glu Ala Asp Phe Ala Lys Arg
 20 25 30

Gly Tyr Lys Leu Pro Lys Val Arg Lys Thr Gly Thr Thr Ile Ala Gly
 35 40 45

Val Val Tyr Lys Asp Gly Ile Val Leu Gly Ala Asp Thr Arg Ala Thr
 50 55 60

Glu Gly Met Val Val Ala Asp Lys Asn Cys Ser Lys Ile His Phe Ile
 65 70 75 80

Ser Pro Asn Ile Tyr Cys Cys Gly Ala Gly Thr Ala Ala Asp Thr Asp
 85 90 95

Met Thr Thr Gln Leu Ile Ser Ser Asn Leu Glu Leu His Ser Leu Ser
 100 105 110

Thr Gly Arg Leu Pro Arg Val Val Thr Ala Asn Arg Met Leu Lys Gln
 115 120 125

Met Leu Phe Arg Tyr Gln Gly Tyr Ile Gly Ala Ala Leu Val Leu Gly
 130 135 140

- 306 -

Gly Val Asp Val Thr Gly Pro His Leu Tyr Ser Ile Tyr Pro His Gly
145 150 155 160

Ser Thr Asp Lys Leu Pro Tyr Val Thr Met Gly Ser Gly Ser Leu Ala
165 170 175

Ala Met Ala Val Phe Glu Asp Lys Phe Arg Pro Asp Met Glu Glu Glu
180 185 190

Glu Ala Lys Asn Leu Val Ser Glu Ala Ile Ala Ala Gly Ile Phe Asn
195 200 205

Asp Leu Gly Ser Gly Ser Asn Ile Asp Leu Cys Val Ile Ser Lys Asn
210 215 220

Lys Leu Asp Phe Leu Arg Pro Tyr Thr Val Pro Asn Lys Lys Gly Thr
225 230 235 240

Arg Leu Gly Arg Tyr Arg Cys Glu Lys Gly Thr Thr Ala Val Leu Thr
245 250 255

Glu Lys Ile Thr Pro Leu Glu Ile Glu Val Leu Glu Glu Thr Val Gln
260 265 270

Thr Met Asp Thr Ser
275

<210> 145

<211> 972

<212> PRT

<213> Homo sapeins

<400> 145

Met Gly Pro Gly Val Leu Leu Leu Leu Val Ala Thr Ala Trp His
1 5 10 15

Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
20 25 30

Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
35 40 45

- 307 -

Glu Trp Asp Gly Pro Ala Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
50 55 60

Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65 70 75 80

Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
85 90 95

Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
100 105 110

Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
115 120 125

Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
130 135 140

Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145 150 155 160

Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
165 170 175

Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
180 185 190

Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val
195 200 205

Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
210 215 220

Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225 230 235 240

Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
245 250 255

Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
260 265 270

Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
275 280 285

-308-

Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser
290 295 300

Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305 310 315 320

Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
325 330 335

Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
340 345 350

Asn Ala Thr Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu
355 360 365

Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
370 375 380

Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr
385 390 395 400

Pro Pro Glu Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr
405 410 415

Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
420 425 430

Gln Cys Ser Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
435 440 445

Val Trp Asp Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His
450 455 460

Lys Val Thr Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn
465 470 475 480

Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
485 490 495

Ala Phe Ile Pro Ile Ser Ala Gly Ala His Thr His Pro Pro Asp Glu
500 505 510

Phe Leu Phe Thr Pro Val Val Val Ala Cys Met Ser Ile Met Ala Leu

- 309 -

515					520					525				
Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Tyr	Lys	Tyr	Lys	Gln	Lys	Pro
530					535					540				
Lys	Tyr	Gln	Val	Arg	Trp	Lys	Ile	Ile	Glu	Ser	Tyr	Glu	Gly	Asn
545					550					555				560
Tyr	Thr	Phe	Ile	Asp	Pro	Thr	Gln	Leu	Pro	Tyr	Asn	Glu	Lys	Trp
				565					570					575
Phe	Pro	Arg	Asn	Asn	Leu	Gln	Phe	Gly	Lys	Thr	Leu	Gly	Ala	Gly
			580					585					590	Ala
Phe	Gly	Lys	Val	Val	Glu	Ala	Thr	Ala	Phe	Gly	Leu	Gly	Lys	Glu
		595					600					605		Asp
Ala	Val	Leu	Lys	Val	Ala	Val	Lys	Met	Leu	Lys	Ser	Thr	Ala	His
610					615					620				Ala
Asp	Glu	Lys	Glu	Ala	Leu	Met	Ser	Glu	Leu	Lys	Ile	Met	Ser	His
625					630					635				640
Gly	Gln	His	Glu	Asn	Ile	Val	Asn	Leu	Leu	Gly	Ala	Cys	Thr	His
				645					650					655
Gly	Pro	Val	Leu	Val	Ile	Thr	Glu	Tyr	Cys	Cys	Tyr	Gly	Asp	Leu
			660					665					670	Leu
Asn	Phe	Leu	Arg	Arg	Lys	Ala	Glu	Ala	Met	Leu	Gly	Pro	Ser	Leu
		675					680					685		Ser
Pro	Gly	Gln	Asp	Pro	Glu	Gly	Gly	Val	Asp	Tyr	Lys	Asn	Ile	His
690					695					700				Leu
Glu	Lys	Lys	Tyr	Val	Arg	Arg	Asp	Ser	Gly	Phe	Ser	Ser	Gln	Gly
705					710					715				720
Asp	Thr	Tyr	Val	Glu	Met	Arg	Pro	Val	Ser	Thr	Ser	Ser	Asn	Asp
				725					730					735
Phe	Ser	Glu	Gln	Asp	Leu	Asp	Lys	Glu	Asp	Gly	Arg	Pro	Leu	Glu
			740					745					750	Leu

- 310 -

Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
755 760 765

Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
770 775 780

Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
785 790 795 800

Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
805 810 815

Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
820 825 830

Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
835 840 845

Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
850 855 860

Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
865 870 875 880

Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
885 890 895

Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
900 905 910

Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
915 920 925

Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu
930 935 940

Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
945 950 955 960

Gln Pro Leu Leu Gln Pro Asn Asn Tyr Gln Phe Cys
965 970

<210> 146

-311-

<211> 397

<212> PRT

<213> Homo sapiens

<400> 146

Met Asn Ala Gly Ser Asp Pro Val Val Ile Val Ser Ala Ala Arg Thr
1 5 10 15

Ile Ile Gly Ser Phe Asn Gly Ala Leu Ala Ala Val Pro Val Gln Asp
20 25 30

Leu Gly Ser Thr Val Ile Lys Glu Val Leu Lys Arg Ala Thr Val Ala
35 40 45

Pro Glu Asp Val Ser Glu Val Ile Phe Gly His Val Leu Ala Ala Gly
50 55 60

Cys Gly Gln Asn Pro Val Arg Gln Ala Ser Val Gly Ala Gly Ile Pro
65 70 75 80

Tyr Ser Val Pro Ala Trp Ser Cys Gln Met Ile Cys Gly Ser Gly Leu
85 90 95

Lys Ala Val Cys Leu Ala Val Gln Ser Ile Gly Ile Gly Asp Ser Ser
100 105 110

Ile Val Val Ala Gly Gly Met Glu Asn Met Ser Lys Ala Pro His Leu
115 120 125

Ala Tyr Leu Arg Thr Gly Val Lys Ile Gly Glu Met Pro Leu Thr Asp
130 135 140

Ser Ile Leu Cys Asp Gly Leu Thr Asp Ala Phe His Asn Cys His Met
145 150 155 160

Gly Ile Thr Ala Glu Asn Val Ala Thr Lys Trp Gln Val Ser Arg Glu
165 170 175

Asp Gln Asp Lys Val Ala Val Leu Ser Gln Asn Arg Thr Glu Asn Ala
180 185 190

Gln Lys Ala Gly His Phe Asp Lys Glu Ile Val Pro Val Leu Val Ser

- 312 -

195	200	205
Thr Arg Lys Gly Leu Ile Glu Val Lys Thr Asp Glu Phe Pro Arg His 210 215 220		
Gly Ser Asn Ile Glu Ala Met Ser Lys Leu Lys Pro Tyr Phe Leu Thr 225 230 235 240		
Asp Gly Thr Gly Thr Val Thr Pro Ala Asn Ala Ser Gly Ile Asn Asp 245 250 255		
Gly Ala Ala Ala Val Ala Leu Met Lys Lys Ser Glu Ala Asp Lys Arg 260 265 270		
Gly Leu Thr Pro Leu Ala Arg Ile Val Ser Trp Ser Gln Val Gly Val 275 280 285		
Glu Pro Ser Ile Met Gly Ile Gly Pro Ile Pro Ala Ile Lys Gln Ala 290 295 300		
Val Thr Lys Ala Gly Trp Ser Leu Glu Asp Val Asp Ile Phe Glu Ile 305 310 315 320		
Asn Glu Ala Phe Ala Ala Val Ser Ala Ala Ile Val Lys Glu Leu Gly 325 330 335		
Leu Asn Pro Glu Lys Val Asn Ile Glu Gly Gly Ala Ile Ala Leu Gly 340 345 350		
His Pro Leu Gly Ala Ser Gly Cys Arg Ile Leu Val Thr Leu Leu His 355 360 365		
Thr Leu Glu Arg Met Gly Arg Ser Arg Gly Val Ala Ala Leu Cys Ile 370 375 380		
Gly Gly Gly Met Gly Ile Ala Met Cys Val Gln Arg Glu 385 390 395		

<210> 147

<211> 390

<212> PRT

<213> Homo sapiens

- 313 -

<400> 147

Met Asp Phe Trp Leu Trp Pro Leu Tyr Phe Leu Pro Val Ser Gly Ala
 1 5 10 15

Leu Arg Ile Leu Pro Glu Val Lys Val Glu Gly Glu Leu Gly Gly Ser
 20 25 30

Val Thr Ile Lys Cys Pro Leu Pro Glu Met His Val Arg Ile Tyr Leu
 35 40 45

Cys Arg Glu Met Ala Gly Ser Gly Thr Cys Gly Thr Val Val Ser Thr
 50 55 60

Thr Asn Phe Ile Lys Ala Glu Tyr Lys Gly Arg Val Thr Leu Lys Gln
 65 70 75 80

Tyr Pro Arg Lys Asn Leu Phe Leu Val Glu Val Thr Gln Leu Thr Glu
 85 90 95

Ser Asp Ser Gly Val Tyr Ala Cys Gly Ala Gly Met Asn Thr Asp Arg
 100 105 110

Gly Lys Thr Gln Lys Val Thr Leu Asn Val His Ser Glu Tyr Glu Pro
 115 120 125

Ser Trp Glu Glu Gln Pro Met Pro Glu Thr Pro Lys Trp Phe His Leu
 130 135 140

Pro Tyr Leu Phe Gln Met Pro Ala Tyr Ala Ser Ser Ser Lys Phe Val
 145 150 155 160

Thr Arg Val Thr Thr Pro Ala Gln Arg Gly Lys Val Pro Pro Val His
 165 170 175

His Ser Ser Pro Thr Thr Gln Ile Thr His Arg Pro Arg Val Ser Arg
 180 185 190

Ala Ser Ser Val Ala Gly Asp Lys Pro Arg Thr Phe Leu Pro Ser Thr
 195 200 205

Thr Ala Ser Lys Ile Ser Ala Leu Glu Gly Leu Leu Lys Pro Gln Thr
 210 215 220

- 314 -

Pro Ser Tyr Asn His His Thr Arg Leu His Arg Gln Arg Ala Leu Asp
225 230 235 240

Tyr Gly Ser Gln Ser Gly Arg Glu Gly Gln Gly Phe His Ile Leu Ile
245 250 255

Pro Thr Ile Leu Gly Leu Phe Leu Leu Ala Leu Leu Gly Leu Val Val
260 265 270

Lys Arg Ala Val Glu Arg Arg Lys Ala Leu Ser Arg Arg Ala Arg Arg
275 280 285

Leu Ala Val Arg Met Arg Ala Leu Glu Ser Ser Gln Arg Pro Arg Gly
290 295 300

Ser Pro Arg Pro Arg Ser Gln Asn Asn Ile Tyr Ser Ala Cys Pro Arg
305 310 315 320

Arg Ala Arg Gly Ala Asp Ala Ala Gly Thr Gly Glu Ala Pro Val Pro
325 330 335

Gly Pro Gly Ala Pro Leu Pro Pro Ala Pro Leu Gln Val Ser Glu Ser
340 345 350

Pro Trp Leu His Ala Pro Ser Leu Lys Thr Ser Cys Glu Tyr Val Ser
355 360 365

Leu Tyr His Gln Pro Ala Ala Met Met Glu Asp Ser Asp Ser Asp Asp
370 375 380

Tyr Ile Asn Val Pro Ala
385 390

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
17 April 2003 (17.04.2003)

PCT

(10) International Publication Number
WO 2003/031650 A3

(51) International Patent Classification⁷: C12Q 1/68,
C07K 14/47, C12N 15/12, 15/11, A61K 48/00

SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number:
PCT/EP2002/011034

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

(22) International Filing Date: 2 October 2002 (02.10.2002)

(25) Filing Language: English

(26) Publication Language: English

Declaration under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ,
VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS,
MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG)

(30) Priority Data:
0124145.4 8 October 2001 (08.10.2001) GB

(71) Applicant (*for all designated States except US*): BAYER
HEALTHCARE AG [DE/DE]; 51368 Leverkusen (DE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MUNNES, Marc
[DE/DE]; Am Schimmelskämpchen 14, 40699 Erkrath
(DE). GEHRMANN, Mathias [DE/DE]; Alte Landstr.
140, 51373 Leverkusen (DE). WICK, Maresa [DE/DE];
Engeldamm 62, 10179 Berlin (DE). SCHMITZ, Gerd
[DE/DE]; Turmstr. 15a, 93161 Sinzing (DE).

(74) Common Representative: BAYER HEALTHCARE
AG; 51368 Leverkusen (DE).

Published:

— with international search report

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,

(88) Date of publication of the international search report:
12 February 2004

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: GENES AND PROTEINS FOR PREVENTION, PREDICTION, PROGNOSIS AND THERAPY OF CARDIOVASCULAR DISEASE

(57) Abstract: Genes that are differentially expressed in blood vessels of cardiovascular disease patients versus blood vessels of normal people are disclosed. The genes provide novel methods, uses and compositions for the prediction, prevention, diagnosis, prognosis and treatment of cardiovascular disease.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/11034

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 C07K14/47 C12N15/12 C12N15/11 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, SEQUENCE SEARCH, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 72774 A (MIDGLEY CAROL ;CYCLACEL LTD (GB); DEAK PETER (GB); GLOVER DAVID MO) 4 October 2001 (2001-10-04) page 6, line 7-11 page 41, line 14-18 ---	1-3, 5-11,13
X	US 6 087 117 A (STEEG PATRICIA SCHRIVER ET AL) 11 July 2000 (2000-07-11) the whole document ---	5,6,13
A	BARRANS ET AL.: "Construction of a human cardiovascular cDNA microarray: portrait of the failing heart" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 280, January 2001 (2001-01), pages 964-969, XP002248512 the whole document --- -/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

22 July 2003

Date of mailing of the international search report

12.11.2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bort, S

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/11034

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MCCAFFREY ET AL.: "High-level of expression of Egr-1 and Egr-1-inducible genes in mouse and human atherosclerosis" THE JOURNAL OF CLINICAL INVESTIGATION, vol. 105, no. 5, March 2000 (2000-03), pages 653-662, XP002248513 abstract</p> <p>---</p>	
A	<p>LAWN ET AL.: "The Tangier disease gene product ABC1 controls the cellular apolipoprotein-mediated lipid removal pathway" THE JOURNAL OF CLINICAL INVESTIGATION, vol. 104, no. 8, October 1999 (1999-10), pages R25R-R31, XP002248514 abstract</p> <p>-----</p>	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/11034

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-3 (partially), 14
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 4, 12
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-3, 5-11, 13 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 1-3 (partially), 14

Claims 1-3 are directed to a diagnostic method practised on the human/animal body. According to Rule 39.1(iv) PCT, subject-matter regarding methods for treatment of the human/animal body is not required to be searched. Notwithstanding the mentioned objection, the search has been carried out and based on the alleged effects of the sequences claimed.

Claim 14 refers a computer readable medium, which are merely physical entities for the presentation of information. According to Rule 39.1(v) PCT subject-matter regarding presentation of information is not required to be searched. Therefore, claim 14 has not been searched.

Continuation of Box I.2

Claims Nos.: 4, 12

Claim 4 refers to a diagnostic kit defined by reference to a desirable characteristic or property, namely a diagnostic kit for conducting the method of any of claims 1-3. The claim covers all diagnostic kits having this property, whereas the application does not provide support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT therefor. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independently of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the reagent by reference to a result to be achieved. Again, this lack of clarity in the present case renders a meaningful search over the whole claimed scope impossible. Moreover, the search could not even been carried out for those parts of the claim which would appear clear, supported and disclosed, namely the examples, since the present application does not provide examples.

Claim 12 refers to a reagent defined by reference to a desirable characteristic or property, namely a reagent that regulates the activity of the polynucleotides listed in said claim. The claim covers all reagents having this property, whereas the application does not provide support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT therefor. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independently of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the reagent by reference to a result to be achieved. Again, this lack of clarity in the present case renders a meaningful search over the whole claimed scope impossible. Moreover, the search could not even been carried out for those parts of the claim which would appear clear, supported and disclosed, namely the examples, since

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

the present application does not provide examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-3, 5-11, 13 (all partially)

Invention 1

(Pharmaceutical) Composition and array comprising a polynucleotide (or derivatives) comprising SEQ ID No. 1; methods using them; and use of the polynucleotide (or derivatives) for the preparation of compositions

2. Claims: 1-3, 5-11, 13 (all partially)

Invention 2

(Pharmaceutical) Composition and array comprising a polynucleotide (or derivatives) comprising SEQ ID No. 2; methods using them; and use of the polynucleotide (or derivatives) for the preparation of compositions

Inventions 3-74

Ibidem for SEQ ID Nos. 3-74

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/11034

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0172774	A	04-10-2001	AU 3943401 A	08-10-2001
			EP 1330472 A2	30-07-2003
			WO 0172774 A2	04-10-2001
			US 2003152945 A1	14-08-2003

US 6087117	A	11-07-2000	US 6423836 B1	23-07-2002
			US 6329198 B1	11-12-2001
			AT 206129 T	15-10-2001
			AU 643971 B2	02-12-1993
			AU 7042491 A	16-05-1991
			CA 2067797 A1	19-04-1991
			DE 69033810 D1	31-10-2001
			DE 69033810 T2	28-03-2002
			DK 495910 T3	14-01-2002
			EP 0495910 A1	29-07-1992
			ES 2164634 T3	01-03-2002
			JP 3295358 B2	24-06-2002
			JP 10212299 A	11-08-1998
			JP 2758500 B2	28-05-1998
			JP 4506457 T	12-11-1992
			WO 9105793 A1	02-05-1991
			US 5753437 A	19-05-1998

Form PCT/ISA/210 (patent family annex) (July 1992)